Organising HIV ageing-patient care in South Africa: An implementation science approach

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The rollout of efficient antiretroviral therapy in many countries, including South Africa (SA), has transformed HIV into a manageable chronic condition, and led to rising life expectancies among people living with HIV/AIDS. As a result, in Africa and elsewhere, there have been a number of reports on multiple comorbidities from non-communicable diseases in those living and ageing with HIV.
We conducted a desktop review of studies conducted in SA and other countries on medical service administration and organisation, and planning of interventions aimed at people ageing with HIV, and acquiring non-communicable diseases due to ageing. Furthermore, older adults with HIV have, as a group, unique issues relating to medication compliance, and are more likely to have issues such as polypharmacy and cognitive impairment.
One approach to tackling these issues could be an integrated care, instead of a specialised clinical approach. However, an integrated approach requires a strong commitment from all parties, investment in patient and clinician education and relationship management among providers, services and funders. Although there is no doubt that great progress has been made in extending services for HIV prevention, care and treatment in the last decade, substantial gaps remain in terms of what we know is working, and what we are really achieving with the various programmes. To address this issue, we suggest the use of an implementation science framework, to improve the efficiency and effectiveness of these programmes. Policy- and decision-makers in SA and other parts of Africa will need to put further concerted effort and greater emphasis on targeted care, in particular for older adults.

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The number of HIV-infected individuals in South Africa (SA) was estimated by the Joint United Nations Programme on HIV and AIDS (UNAIDS) to be between 6.4 million and 7.8 million in 2016,[1] with an infection-rate prevalence of 16.6% - 21.0% among the population aged 15 - 49 years.

In terms of the management of the infection, in relation to the 90-90-90 treatment cascade, in 2016, UNAIDS estimated that the mean percentage of infected people aware of their status was 86% (between 78% and 95%); of these people, 65% (between 59% and 72%) were receiving antiretroviral treatment (ART); and the mean percentage of patients receiving ART with viral suppression was 81% (between 74% and 89%).[1]

In 2016, in SA, the most common cause of premature death was HIV/AIDS (and also the most common cause of death overall), with a 50.6% decrease from 2005, while diabetes was the sixth most common cause of premature death (fourth of the overall causes of death), with an increment of +5.3% since 2005, while ischaemic heart disease was the seventh most common cause of premature death (second of the overall causes of death) with a 10.9% decrease since 2005.[2] In terms of disability-adjusted life years, in 2016, HIV/AIDS was the most common cause of death and disability combined, diabetes the sixth-most, and ischaemic heart disease the seventh.[2]

This data shows how the combination of these pathologies and risk factors might lead to an increased complexity of patient conditions.

Chronic diseases and HIV burden

According to Young *et al.*,[3] ART for HIV is associated with an increased risk of developing metabolic syndrome (a cluster of obesity, hyperglycaemia, dyslipidaemia and hypertension), and therefore also a predisposition to type 2 diabetes and cardiovascular disease.

Aboud *et al.*[4] found that insulin resistance is common in HIV-infected people, particularly those treated with protease inhibitor therapy. The prevalence of hyperglycaemia and diabetes mellitus is significantly higher in people with HIV infection treated with antiretrovirals (ARVs) than in the general population.

Carr *et al.*[5] mention that patients who were HIV protease-inhibitor naive had similar body composition to healthy men, whereas for HIV-infected people treated with protease inhibitor, this was associated with substantially lower total body fat (13.2 v. 18.7 kg

in protease-inhibitor-naive patients; p=0.005), and with significantly higher total cholesterol and triglyceride levels.

Lipodystrophy in HIV-infected patients is associated with insulin resistance and its metabolic complications, such as impaired glucose tolerance, diabetes, hypertriglyceridaemia and low serum high-density lipoprotein cholesterol levels.[6]

The combination of central lipohypertrophy, dyslipidaemia and insulin resistance is associated with accelerated rates of atherosclerosis and other potentially significant long-term effects resulting from highly active antiretroviral therapy (HAART).[7]

Grinspoon *et al*.[8] found that metabolic and body-fat abnormalities are common among HIV-infected adults receiving nucleoside-analogue and protease-inhibitor therapy. There are suggestions that HAART increases risk of cardiovascular disease. Diet, lifestyle modification and use of lipid-lowering and insulin-sensitising regimens may be useful in specific situations.

Pao *et al*.[9] state that people with HIV infection have metabolic abnormalities that resemble metabolic syndrome (hypertriglyceridaemia, low high-density lipoprotein cholesterol and insulin resistance), which are known to predict increased risk of cardiovascular disease (CVD). CVD has become more prominent among HIV-infected individuals. Patients with HIV had significantly higher CVD mortality than the general population in all age groups up until age 65 (based on demographic characteristics such as sex, race/ethnicity and borough of residence).[10] Hanna *et al*.[10] further found that after age 65, CVD mortality rate was similar or greater in the general population compared to that of the HIV population. The CVD mortality rate was highest among viraemic patients, but still elevated among the virally suppressed (<400 copies/mL) compared with the general population.

Age-associated comorbidities (especially cardiovascular and renal disease) were more prevalent among HIV-infected patients than HIV-uninfected patients. Comorbidity was associated with cardiovascular risk factors, but also with HIV infection, immunodeficiency and, to a lesser extent, systemic inflammation and prior high-dose ritonavir use.[11] In comparison with HIV-uninfected controls, all age-associated non-communicable comorbidities (AANCCs), especially peripheral arterial cardiovascular disease and impaired renal function, were more prevalent among HIV-infected participants. In addition to recognised cardiovascular risk factors, HIV infection and longer time spent with severe immunodeficiency increased the risk of a higher composite AANCC burden. However, there was a less pronounced contribution from residual inflammation, immune activation and prior high-dose ritonavir use.

The SA context

In 2011, Julius *et al*.[12] published a monocentric analysis of the prevalence of metabolic diseases among 304 HIV-infected patients of the HIV clinic at the Charlotte Maxeke Johannesburg Academic Hospital, focusing on hypertension, diabetes, obesity and dyslipidaemia. Regarding hypertension, the authors identified a slightly higher prevalence in HIV-infected women than women in the general population, and a twofold higher prevalence in HIV-infected males than males in the general population. Obesity and overweight were less frequent, while lipid metabolism abnormalities, such as hypercholesterolaemia, total cholesterol, low-density lipoprotein cholesterol and triglycerides, were more frequent than in the general population.

The overall clinical condition of HIV-infected patients may therefore lead to further decline owing to concomitant pathologies related to HIV infection, with an increased clinical, humanistic and economic burden for both the patient and the health services. The presence of multiple chronic pathologies would have clinical consequences in terms of decreased quality of life for the patients, and both higher direct medical costs and indirect costs to the health service due to the provision of healthcare services, and lower working capacity, respectively, leading to absenteeism and further productivity loss in caregivers.

Patients affected by multiple chronic diseases are complex, and it is necessary to implement specific care pathways, to avoid drug interactions and to identify possible synergies in the diagnostic and curative pathways of the affected pathologies. The management of these patients, in fact, might require multiple services for the monitoring and care of each individual pathology, with increasing costs involved in managing possible events related to the clinical evolution of each one.

The costs correlated with the management of diabetes in SA were investigated by Atun *et al*.[13] in 2017, identifying an annual cost per person of USD140 in the public sector, and USD1 400 in the private sector, resulting in high levels of inequity.

The outpatient management of hypertension was estimated in 2001 to lead to a yearly cost per person of USD169.28 (all values at 2012 rates) in SA.[14,15] The costs in SA of further cardiovascular events are reported in the literature as: ischaemic heart disease in terms of coronary artery bypass grafting procedure USD22 500.46 per patient; catheter-based revascularisation inpatient treatment USD9 324.18 per patient; average inpatient treatment direct medical costs, USD11 093.74 per patient; annual per-patient cost for postcoronary heart disease with coronary artery bypass grafting USD2 558.88 the first year, and USD1 181.02 in subsequent years; and the annual per-patient cost for postcoronary heart disease without coronary artery bypass grafting USD2 952.56 the first year, and USD1 653.43 in subsequent years.[14,15]

Regarding stroke, the cost of inpatient visits for stroke care per patient are estimated at USD16 992.95.[14,15]

To manage the increasing level of complexity of patients affected by multiple chronic pathologies, the integration of the care of diabetes and hypertension in HIV care models would improve the management of HIV-infected patients.[13]

The hospital organisation problem: Integrated v. specialised clinical approach

We performed a comparative analysis of both approaches, the integrated and the specialised clinical, to address the problem of organisational (and clinical) appropriateness. The most suitable dimensions of the comparison are patient perception, hospital management, clinical approach and specialised output (Table 1).

Another dimension to consider is the human factor. Doctors have different attitudes, professional capacities and amount of

Table 1. Hospital organisation: Comparative analysis of integrated and specialised clinical approaches

Dimension	Specialised (multiple ambulatories)	Integrated (single ambulatory)
Patient perception	Multiple waiting queues, multiple doctors/nurses in relation to time for overall performance, increased stigma risk	Risk of one single contact, doctor time constraint per single (complicated) visit
Hospital management	Number of doctors (contract, control, performance check), hospital infrastructure (space)	Single doctor relation, long queue
Clinical approach	Follows doctors' attitude; integration of specialised treatment	Doctor with broad specialisation
Specialised output	Multiple	Single

time to dedicate; hence, the choice of hospital organisation is complicated.

Implementation science provides a solution to this challenge. It is the study of methods to promote the integration of research findings and evidence into healthcare policy and practice. Therefore, it supports innovative approaches to identifying, understanding and overcoming barriers to the adoption, adaptation, integration, scale-up and sustainability of evidence-based interventions, tools, policies and guidelines.[16]

Support for implementation science

In the last few decades, the application of clinical research findings to the implementation and dissemination of routine practice, for the benefit of both patients and the public, has come under the spotlight. This reflects the collective realisation that findings from clinical studies have not uniformly resulted in changes in the practices of healthcare providers or patients, nor have they always yielded improvements in health outcomes.[17,18]

Implementation science is the study of what happens after adoption occurs, especially in organisational settings. Typical questions addressed are: where does the current emphasis on dissemination and implementation science come from? How is new media altering the diffusion of new practices, programmes, and beliefs? Collective knowledge of the diffusion-of-innovations paradigm has given way to a focus on those paradigmatic concepts, in purposive tests of how to best disseminate and implement evidence-based health practices, programmes and policies. This has long been an objective in trying to spread effective innovations for improved global health, as well as for domestic healthcare and public health.[19]

The Consolidated Framework for Implementation Research (CFIR) offers an overarching typology to promote implementation theory development, and verification about what works where and why across multiple contexts.[20] The CFIR is composed of five major domains: intervention characteristics, outer setting, inner setting, characteristics of the individuals involved and the process of implementation. Eight constructs compose the intervention area (e.g. evidence strength and quality), four constructs are related to outer setting (e.g. patient needs and resources), twelve constructs are related to inner setting (e.g. culture, leadership engagement), five constructs are related to individual characteristics (e.g. knowledge of and belief about the intervention, self-efficacy, individual stage of change, individual identification with organisation, and other personal traits such as ambiguity or motivation) and eight constructs are related to process (e.g. plan, evaluate and reflect).

Curran *et al*.[21] propose three methods for blending design components of clinical effectiveness and implementation research. For them, an effectiveness-implementation hybrid design is one that uses an *a priori* dual focus in assessing clinical effectiveness and implementation. The proposed hybrid types are: (*i*) testing the effects of a clinical intervention on relevant outcomes, while observing and gathering information on implementation; (*ii*) dual testing of clinical and implementation interventions/strategies; and (*iii*) testing an implementation strategy while observing and gathering information on the clinical intervention's impact on relevant outcomes.

However, implementation science studies have their challenges. Both Link4Health and Engage4Health studies,[22,23] conducted in public HIV programmes in Swaziland and Mozambique, faced difficulties in assessing outcomes owing to incomplete electronic records, missing health records and issues of missing data around parameters such as linkage of care, patients no longer in care and mortality data. Nevertheless, implementation science research results in generalisability, and gives relevance to scalable delivery modes.[25]

Powell *et al*.[17] propose further tools for implementation science strategies, and this comprehensive approach can be adapted to the SA context.

Conclusions and next steps

In the near future, PLHIV will begin to experience numerous complications. The progressive ageing of the HIV-infected population means that an increasing number of patients will have one or more comorbidities not directly related to HIV infection, and/or correlated with the side-effects of drugs.

The clinical complexity of the HIV-infected patient therefore requires a programme of care that can deal with the medical, psychosocial and functional aspects of the disease, as well as all other complications characteristic of elderly persons.[26]

The intensity of treatment (shorter intervals between visits and referrals to multispecialist centres) required for these patients needs to be personalised, through shared pathways between the HIV specialist and other specialists (e.g. cardiovascular and renal).

To manage this trend we suggest two technical solutions: integrated ambulatory care for HIV patients in which doctors and other healthcare professionals manage HIV and the main comorbidities, or different specialised ambulatory care for the main comorbidities. Additionally, robust policy settings, appropriate infrastructure and improved service capabilities need further attention.[25]

Therefore, the evaluation of the patient's clinical picture through the global risk assessment of a particular HIV-associated comorbidity through successive levels of assessment is fundamental, and actions may require specialist intervention.[26]

In hospital organisation, the final decision will depend upon the availability of human resources. Doctors, specialised staff and their

attitudes towards the management of these treatments will make all the difference. Hence, managers will play a key role.

Since 2010, in SA, new HIV infections have decreased by 49%, and AIDS-related deaths by 29%.[1] However, to achieve better outcomes, all partners need to optimise the implementation of existing prevention and treatment interventions, and use tools such as the implementation science framework to measure the efficient utilisation of various resources.

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