



Published in final edited form as:

S Afr Fam Pract (2004). 2019 ; 61(6): 273–275. doi:10.1080/20786190.2019.1657268.

Primary prevention of cardiovascular disease in South African women living with HIV

S Hanley*

Centre for the AIDS Programme of Research in South Africa (CAPRISA), Umlazi Clinical Research Site, Nelson R Mandela School of Medicine, Durban, South Africa

Abstract

The colliding epidemics of HIV and cardiovascular disease (CVD) are of great public health concern. People living with HIV (PLHIV) are more predisposed to CVD development as a result of a multitude of contributors. Women living with HIV (WLHIV) appear to be at a higher risk of developing CVD given a heightened immune activation and, in South Africa particularly, a higher body mass index compared with their male counterparts. The World Health Organization (WHO) has made recommendations for the provision of a CVD risk assessment for all PLHIV and has developed regional CVD prediction charts to identify PLHIV who may require primary prevention strategies by means of interventions such as the WHO Package of Essential Non-communicable Disease Interventions for primary health care in low-resource settings (WHO PEN). However, methods of risk prediction and risk reduction integrated strategies for atherosclerotic CVD in PLHIV such as the WHO PEN, particularly in women who may have sex-specific risk factors and culture-specific perceptions of body image, remain a major research gap in developing countries. Further research is crucial in guiding primary health care policy in South Africa.

Keywords

cardiovascular disease risk; primary prevention; women living with HIV

In South Africa, an estimated 21% of the population aged between 15 and 49 years are living with HIV, of which 26% are women.¹ The introduction of treatment strategies, such as Option B+ and Universal Test and Treat, has led to a marked increase in the uptake of antiretroviral therapy (ART) in women from low- and middle-income countries (LMICs). The result has been a steep decline in the numbers of AIDS-related deaths and a life expectancy comparable to that of the general population.² Longevity is coupled with chronic multimorbidity, which necessitates a transition from the current primary health care (PHC) protocols to an integrated management approach for chronic communicable and non-communicable diseases (NCDs), in particular HIV and chronic diseases that are risk factors for atherosclerotic cardiovascular disease (CVD).³ CVD has been shown to be a leading

cause of death both globally and in South Africa, with the related mortality surpassing that associated with infectious diseases.⁴

Why the colliding epidemics of HIV and CVD? Traditional risk factors for CVD, such as a sedentary lifestyle and unhealthy diet, appear to be more evident in PLHIV in LMICs due to epidemiological transition.^{5,6} Furthermore, HIV acts directly through mechanisms of persistent immune activation and chronic inflammation, substantially increasing CVD risk.^{7,8} Immune activation and inflammation have been shown to be more pronounced in women living with HIV (WLHIV), possibly related to sex hormonal differences.^{9,10} Additionally, similar to the protease inhibitors (PIs), the majority of the first-line antiretroviral medication, mainly the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz, and NRTIs currently in use, are shown to cause lipid and vascular endothelial changes.⁷ A combination of these exacerbating factors has led to a surge in the prevalence of metabolic syndrome, with the mean prevalence among PLHIV in Africa being 30.5%.¹¹ Metabolic syndrome, which is defined by abdominal obesity, elevated blood pressure (BP), glucose and dyslipidaemia, doubles the risk of CVD.¹²

Local data indicate that obesity is more pronounced in black females compared with males.¹³ Furthermore, significant weight gain was noted with the use of dolutegravir and tenofovir alafenamide fumarate in South African women in the ADVANCE trial.¹⁴ Investigators have further demonstrated that South Africa is facing an epidemic of hypertension, the most predominant CVD risk factor worldwide.¹⁵ There is a high prevalence of concurrent hypertension in PLHIV.¹⁶ Some 40% of PLHIV were uncontrolled on hypertensive therapy in South Africa.¹⁷ Recognising that the risk of developing CVD is substantially augmented in PLHIV, the World Health Organization (WHO) has made recommendations for the provision of a CVD risk assessment for all PLHIV based on the standard protocols for the general population.¹⁸ However, the commonly used CVD risk assessment tools such as the Framingham table, which is advised by the South African dyslipidaemia guidelines for use at ART initiation, underestimate risk in this relatively younger population, and are non-specific to LMICs.¹⁹

In light of this, the WHO and International Society of Hypertension (WHO/ISH) have developed cardiovascular risk prediction charts specific to 14 epidemiological sub-regions, including Southern Africa.²⁰ A 10-year risk of a cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status and presence of diabetes mellitus can be calculated using WHO/ISH at PHC level. In the author's opinion, this is a valuable tool in identifying PLHIV who may require primary prevention strategies by means of interventions such as the WHO PEN.²¹

The WHO PEN incorporates the WHO/ISH screening and intervention through lifestyle modification and prompt treatment of identifiable CVD risk factors. Studies assessing the WHO PEN intervention in the general population have shown that it is a feasible management plan in reducing CVD risk.²² In an ongoing intervention trial, which focuses on the prevalence and incidence of CVD in WLHIV receiving the WHO PEN intervention, unpublished baseline data reveal that a cohort of South African women of African descent have a high body mass index (mean BMI 29.6 kg/m²). What is interesting to note is that the

majority of WLHIV are satisfied with their current body image. This being the case, it would be beneficial to explore the reasons for this and to further determine the adherence to the recommended intervention that is aimed at achieving a healthy lifestyle, which includes a normal BMI, in future research.

Despite all that is known, there has been slow progress in the introduction of integration in HIV management and CVD prevention and management guidelines in South Africa. Encouraging news is that the pending new 2019 national ART clinical guidelines recommend a BP measurement, urinalysis for glucose and protein, and include the determination of cardiovascular risk, all to be assessed at baseline.²³ However, a fasting cholesterol and triglycerides blood test is only advised if the individual requires a PI-based regimen, and not guided by CVD risk. Thereafter there is no recommendation for CVD screening of persons on ART in follow-up. The PHC Essential Medicines Lists (EML) contains dedicated chapters on HIV management and CVD screening in one convenient tool and the reference to and refresher training of the EML should be an essential and ongoing process at facility level. Other integrated care models such as the Integrated Chronic Disease Management Model (ICDM) is at a pilot and programme implementation level in South Africa. This model aims to address all chronic diseases, not specifically HIV and NCD integration. Preliminary evaluation of the ICDM has demonstrated inadequate infrastructure such as BP machine and staff shortages, and increased patient waiting time.²⁴

Women appear to be at higher risk for CVD given their high BMI and enhanced immune activation compared with their male counterparts. Chronic diseases are becoming progressively more evident in women of reproductive age, placing them at high risk of pregnancy-related morbidity in settings where maternal mortality remains a significant concern. Methods of risk prediction and risk reduction integrated strategies for atherosclerotic CVD in PLHIV, particularly in women who may have sex-specific risk factors and culture-specific perceptions of body image, remain a major research gap in developing countries. Further research is crucial in guiding primary health care policy in South Africa.

Acknowledgments

Funding. (DRILL) Fogarty International Center (FIC), NIH Common Fund, Office of Strategic Coordination, Office of the Director (OD/ OSC/CF/NIH), Office of AIDS Research, Office of the Director (OAR/NIH), National Institute of Mental Health (NIMH/ NIH) of the National Institutes of Health under Award Number D43TW010131.

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