# Cardiovascular disease and HIV

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## Abstract

Among the many comorbidity conditions, cardiovascular disease (CVD) has become an area of particular concern in the field of HIV. The high prevalence of cardiovascular risk factors in people living with HIV, alongside the growing evidence of HIV-accelerated inflammatory processes, known to promote atherosclerosis, presents an ongoing challenge. A good understanding of CVD is, therefore, important for all nurses working in the field of HIV. A sound knowledge and understanding of this area will enhance the nurses' ability to provide holistic, person-centred screening and interventions that strive to improve well-being, quality of life and life expectancy. This article has been prepared to aid your continuing professional development and with revalidation in mind.

**Keywords:** cardiovascular disease, atherosclerosis, HIV disease, antiretroviral therapy, modifiable risk factors, risk reduction

## A. Revalidation

This article has been prepared to aid your continuing professional development and with revalidation in mind. It is estimated that 4 hours of CPD activity will be required for completion of the reading, 'Time out' activities, the quiz and writing a reflective account in relation to your learning and its applicability to your practice. (You could test your knowledge by completing the self-assessment quiz before reading the article, returning to it afterwards to see how much you have learned.)

## B. Aims and intended learning outcomes

This article aims to provide nurses working in HIV care with relevant information on the prevalence and processes of CVD (in particular those associated with HIV), risk factors, screening, prevention and risk-reduction strategies. The role of the nurse in this area will be discussed. After reading this article and completing the activities you should be able to:

- Describe the underlying disease processes understood to cause CVD, in particular that of atherosclerosis;
- List a range of risk factors for CVD, elaborating on current understandings as well as areas of contention;
- Outline the current research findings explaining how HIV infection contributes to the development of CVD;
- Discuss a range of factors that enhance or reduce risk of CVD for people living with HIV (PLWH).
- Evaluate a range of evidence-based risk-reduction strategies and their applicability for your own area of practice; and
- Discuss the role of the nurse in identifying, assessing and supporting those at risk of CVD, including the use of screening tools and behavioural change interventions.

## C. What is cardiovascular disease?

CVD is defined as any disease of the heart or blood vessels, including cardiomyopathy, coronary artery disease, peripheral vascular disease and other conditions, such as rheumatic heart disease, congenital valve disorders, arrhythmias and stroke. The underlying mechanisms of disease can vary. In rheumatic heart disease, for example, damage to the heart muscle and heart valves is caused by infection following a streptococcal pharyngitis/tonsillitis. CVD can also be a symptom of certain syndromes such as the relatively common Wolffe–Parkinson–White syndrome, which causes episodes of cardiac arrhythmia, usually superventricular tachycardia. In congenital heart disease malformations of heart structures are present at birth and may be caused by maternal infections (e.g. rubella), maternal use of alcohol and/or some drugs (e.g. warfarin), or maternal deficiency of folic acid, among other causes. Different types of cardiovascular diseases are shown in Figure 1.

This article will focus largely on CVDs related to atherosclerosis, that is predominantly on coronary/ischaemic heart disease.

## D. Cardiovascular disease: prevalence in the general population

Cardiovascular diseases, primarily coronary artery and cerebrovascular disease are the leading cause


***Figure 1:*** *Different types of cardiovascular diseases.*

of death, globally, and this is true in all areas of the world except Africa [1]. Deaths due to these conditions rose to 17.3 million worldwide in 2013 (accounting for 31.5% of deaths), an increase of 5 million since 1990 [2].

In 2014 in the UK, CVD caused 27% of all deaths, second only to cancer. However, between 1980 and 2013, age-standardised CVD death rates declined by around 70%, albeit with some regional variables [3]. This is thought to be due to a number of factors such as improved disease screening, improved medical management of underlying risk factors (such as hypertension and hypercholesterolaemia), a reduction in the number of smokers together with advances in clinical management following related events such as myocardial infarction (MI) and cerebrovascular accident (CVA) or stroke [4].

Most cardiovascular disease affects middle- and older-aged adults. In the United States, for example, 37% of people between the ages of 40 and 60 and 71% of people aged between 60 and 80 have CVD [5]. Disease onset is typically 7–10 years earlier in men compared to women [1].

**Time out activity 1**

Review the latest British Heart Foundation Report showing the UK burden of CVD by age and gender, as well as regional and national figures [3].

In addition, the report contains latest mortality and morbidity statistics, plus datasets for costs and treatments and trends over time (available at: www.bhf.org.uk/publications/statistics/cvd-stats-2015).

## E. The process of atherosclerotic disease

The underlying disease process that results in coronary heart disease and cerebrovascular disease is known as atherosclerosis. Atherosclerosis affects medium- and large-sized blood vessels throughout the cardiovascular system. Over recent decades it has become increasingly clear that the process is not just a matter of cholesterol passively building up in the arteries, but one that involves an active inflammatory process.

The endothelium of these blood vessels is exposed to high levels of low-density lipoprotein cholesterol (LDL cholesterol), resulting in permeability to certain white blood cells, which then move and embed in the deeper layers of the vessel wall. LDL cholesterol particles are further attracted to these sites and macrophages respond. In addition, smooth muscle cells also move from the media layer. A fibrous cap is formed and when the macrophages begin to die a necrotic core develops underneath this cap. Lesions form, known as atheromatous plaques, which enlarge over time and begin to bulge, narrowing the lumen. Other inflammatory chemicals act to weaken the

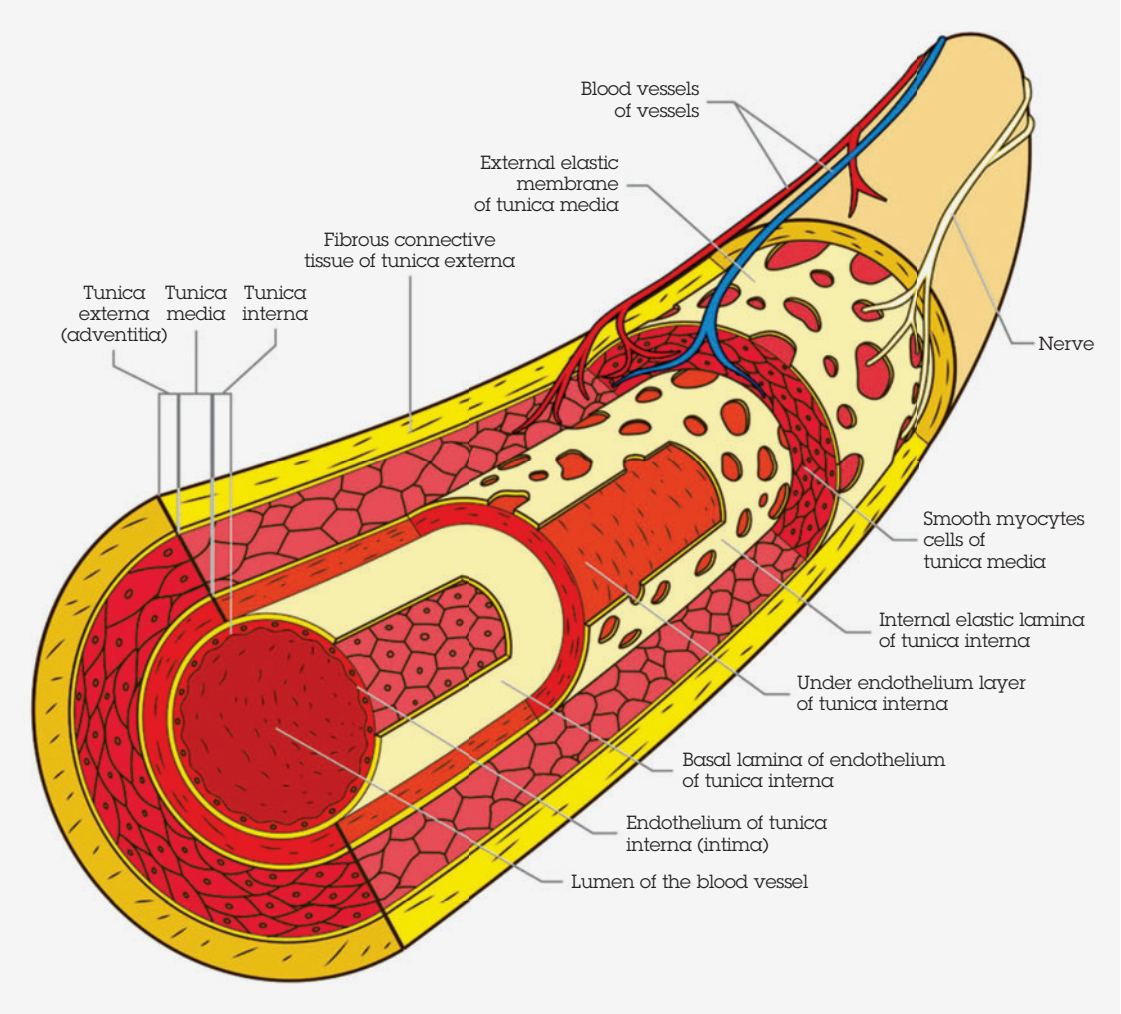


***Figure 2:*** *Structure of an artery*

cap, ultimately causing it to rupture. Lipid fragments and cellular waste are released into the vessel lumen, and, assisted by fibrinogen, result in the formation of a clot. The clots are then broken down by plasminogen, releasing a protein-based by-product called D-dimer. Pieces of these plaques or clots can break away causing a coronary artery or a cerebral blood vessel to become partially or completely occluded, resulting in so-called 'CVD events' such as myocardial infarction (MI) or cardiovascular accident (CVA).

**Time out activity 2**

Refresh your memory of the structure of arteries and the basics of the process of atherosclerosis by studying Figures 2 and 3.

## F. Markers of CVD

Intima or intima-media thickness (IMT) is used to detect the presence of atherosclerotic disease in humans and also to track progression or regression of this disease process. The tunica intima and tunica media are the innermost two layers of the wall of an artery and IMT is a measurement of the depth of these two layers. The measurement is usually made by external ultrasound. Carotid artery IMT (CIMT) has also been measured in numerous clinical studies. Increased readings have been shown to be associated with numerous risk factors, including type 2 diabetes, impaired glucose tolerance and hypercholesterolaemia [6].

Although IMT has been shown to be predictive of future cardiovascular events, meta-analysis has found that changes in IMT are **not** predictive, therefore, the use of this test as an endpoint in clinical trials, and also in the management of cardiovascular disease, is controversial and unclear [7]. Importantly, although IMT is strongly associated with atherosclerosis, thickening of the intima media may not always be due to this. The process depends on a variety of factors, including haemodynamics and blood pressure, amongst other influencing factors.

Another significant process believed to contribute to the development of CVD is generalised inflammation. It is well established that this is a major factor in the

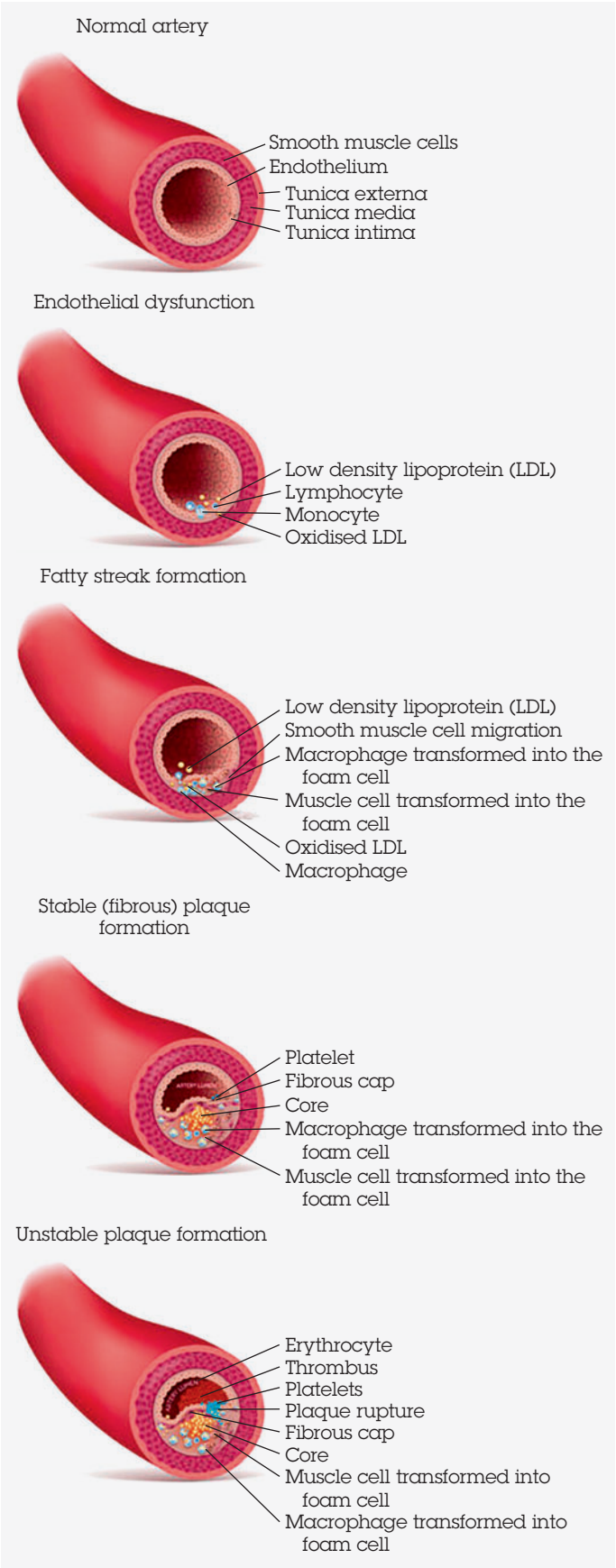


***Figure 3:*** *The process of atherosclerosis*

development of atherosclerosis in the general population [8], and a variety of inflammatory markers have been shown to predict CVD. For example, elevated C-reactive protein (CRP) and interleukin-6 (IL-6) values are both predictors of CVD events in the general population [9].

## G. Predictive markers of CVD in PLWH

There is some evidence that increasing levels of some inflammatory markers such as CRP are associated with HIV disease progression and negative disease outcomes; however, the bulk of evidence to date in relation to their significance as possible predictors of CVD, in association with HIV, has been inconsistent [10].

CIMT as a surrogate marker for atherosclerosis has been associated with vascular inflammation in PLWH [11]; and research has shown that these individuals are at increased risk of progression of coronary artery disease as well, when compared with sex- and age-matched controls [12].

Box 1 summarises the findings of a recent and useful systematic review of 40 articles [13] that had published research in relation to inflammatory markers and the relevance of CIMT on cardiovascular disease in PLWH.

**Box 1. Summary of findings from a systematic review of 40 articles**

- CRP, IL-6 and D-dimer were assessed most frequently in relation to the occurrence of CVD.
- These three markers were positively related to CVD in three out of four studies.
- None of the inflammatory markers showed an association with CIMT.
- Studies addressing CIMT were too heterogeneous with respect to patient populations, inflammatory markers, measurement protocols and statistical methods, to allow for a formal meta-analysis.
- Further research should focus on prospective studies and a specific set of inflammatory markers.

Source: Vos *et al.* 2016 [13].

A further test – baseline coronary artery calcification (CAC) has been shown to accurately identify coronary atherosclerosis [14], but it is still unclear whether knowledge of any changes over time to this test score in an individual improves risk prediction. Research continues to explore whether the slowing of CAC progression with therapeutic interventions such as statin use provides prognostic benefits.

## H. The role of inflammation

The role of inflammation in the development of cardiovascular disease in the general population has been clearly demonstrated [8]. Immune cells respond to early atherosclerotic lesions, accelerating the progression of the lesions and activating the inflammatory response. In those with HIV infection, it is thought that the early damage to arterial endothelial cells may be exacerbated by HIV proteins,

which alter cell-signalling pathways, in turn contributing to endothelial dysfunction. Furthermore, it is thought that raised CRP may have a direct effect on endothelial function.

The Strategies for Management of Antiretroviral Therapy (SMART) study [15] reported that elevated levels of some inflammatory biomarkers were strongly associated with increased cardiovascular-related deaths in PLWH. Inflammatory markers rose after treatment interruption but they remained stable in people who took continuous therapy. The investigators noted that people with the highest CRP values were twice as likely to die as those with the lowest levels. Furthermore, those with the highest IL-6 and D-dimer values also had a significantly greater risk of death. In addition, results from another treatment interruption study, the STACCATO trial, demonstrated a link between viral suppression and biomarkers associated with inflammation and endothelial dysfunction [16].

The inflammatory process also helps explain the effects of some of traditional cardiovascular disease risk factors. Excess body fat produces pro-inflammatory compounds and smoke from cigarettes contains toxins that promote inflammation. LDL cholesterol build-up in artery walls triggers inflammatory responses. Of note, HDL cholesterol removes LDL from the arteries and has an anti-inflammatory effect.

## I. Untreated HIV disease and CVD – what do we know?

As we have seen in the previous section, research has sought to try and clarify links between an elevation in markers of systemic inflammation and immune system activation and cardiovascular function and disease. However, most earlier research was undertaken among individuals who had already been treated with ART, which made it difficult to determine the extent and proportion of the influence on CVD risk of HIV itself, the drug therapies used, and to other factors.

The role of untreated HIV infection as an independent variable was, however, clearly demonstrated by the previously mentioned SMART study [15]. Participants who were randomly allocated to the drug conservation arm (i.e. intermittent treatment guided by CD4 cell counts) had a 60% increased risk of CVD during the study period, compared with those with viral suppression on the continuous therapy arm of the study. It was therefore proposed that a combination of unsuppressed HIV viral load, immunological factors and inflammation (all because of discontinuing ART), contributed to enhanced CVD risk.

The specific link between immunodeficiency and CVD is still unclear with study findings being inconsistent. For example, the D:A:D study consistently reported no association between immunodeficiency and CVD risk [17]; the Aquitaine study that investigated hospitalisation rates between 2000 and 2004 among PLWH found little association [18]. On the other hand, the HIV Outpatient Study (HOPS) [19] cohort reported a 28% increased risk of CVD for people with baseline CD4 cell counts of between 350 and 499 cells/mm$^3$ and a 58% increase for those with a baseline count of <350 (compared with counts >500 cells/mm$^3$). However, of note, it was the current rather than the baseline/nadir CD4 cell count that was found to be relevant.

Interestingly, data from the Concerted Action on Sero-Conversion to AIDS and Death in Europe (CASCADE) study [20] suggested a stronger association with HIV viraemia and CVD-related deaths, than with CD4 cell count. The San Francisco-based SCOPE study found that those with HIV experience more rapid atherosclerosis progression than HIV-negative individuals over 2 years. However, in contrast to CASCADE, this was seen to some extent in people with both detectable and undetectable viral loads on ART and even in elite controllers [21].

**Key point**

The association between immune status, inflammation and CVD risk remains the subject of ongoing research.

## J. Treated HIV disease and CVD – what do we know?

Antiretroviral therapy has led to a dramatic reduction in AIDS-related morbidity and mortality. However, in parallel, there has been an increase in morbidity and mortality not directly related to HIV-related immunosuppression; with CVD being the most prevalent. Approximately 20% of PLWH in developed countries are reported to be at high risk of MI over 10 years, with an additional 9% being at moderate risk over the same time frame [22].

For those living with HIV, the risks of CVD are increased, as we have already seen, due to the inflammatory nature of the disease process itself but risk is also potentially heightened due to ART-induced metabolic changes. In addition, so-called modifiable and lifestyle-associated cardiovascular risk factors are prevalent in the HIV-positive population, which will be discussed further in Section M of this article.

Hemkens and Bucher [23] analysed systematic reviews and the most cited literature published between 2011 and 2014 on HIV and CVD, they concluded that ART may induce dyslipidaemia, reduce insulin sensitivity, and promote body fat redistribution that additionally contributes to CVD risk in PLWH. Furthermore, the analysis concluded that some specific ART drugs may further increase risk for CVD events. However, treatment regimens today largely seek to avoid the use of drugs that are most associated with fat redistribution and glucose abnormalities. Overall the absolute risk increase was reported to be moderate and it must be weighed up in relation to the considerable benefits of timely treatment and sustained viral suppression.

**Key point**

Overall, the most consistent findings lead to the conclusion that, regardless of drug regimen, ART reduces inflammatory and cardiovascular biomarkers compared with no treatment. On balance the consensus is that early initiation of ART is likely to reduce CVD events and offset potential side effects from ART-induced metabolic changes.

This view is further supported by data from the SMART study (see Section H), which demonstrated that ART use resulted in reductions in markers of endothelial and coagulation activation and in improvements in vascular endothelial functioning; and that these changes are at least partially reversible with viral suppression [15].

Importantly, it also now appears that suboptimal ART adherence may be associated with enhanced inflammation and immune activation, despite the apparent suppression of viral load. The authors of a recent study suggest adherence should be a target for future investigations aimed at further reducing residual chronic inflammation and immune activation in PLWH [24].

## K. The role of the ageing process

People with HIV are living longer. The number of people with an HIV diagnosis who are aged over 55 has seen a significant increase over recent years. One in three people accessing HIV care in the UK is now aged 50 or over with 5% being over 65 [25]. However, with this longer life expectancy PLWH exhibit many clinical characteristics commonly observed in ageing, for example multiple chronic diseases or conditions, changes in physical and cognitive abilities, and polypharmacy. An example is the prevalence of hypertension, which increases with age in the general population, also increases as expected for those living with HIV, as demonstrated in the D:A:D study cohort [17]. Studies have also shown that among PLWH, the risk of CVD increases with age, as it does for the HIV-negative population [26].

Between 2% and 14% of PLWH have been diagnosed with diabetes mellitus and other glucose tolerance disorders, and this proportion is increasing over time as the HIV-positive population has aged. Again in the D:A:D study, increasing age was significantly predictive of incidence of glucose-related disorders, even after adjustment for other CVD risk factors, as well as treatment with ART [17].

The MACS study [27] looked at CAC measurements among HIV-positive and HIV-negative men (as mentioned in Section G, this is arguably a predictor of CVD). The study revealed that the prevalence and extent of calcification was most strongly associated with advancing age. Although HIV infection and long-term use of ART increased the likelihood of CAC among those with existing calcification, men who were taking ART had this to a lesser extent.

Dyslipidaemia is also associated with ageing in the general population. In one large US study of middle-aged and older people of multi-ethnic background without pre-existing clinical CVD, almost one-third of those studied had drug treatment-eligible lipid abnormalities [28]. Of note, dyslipidaemia was more common in men than in women in this study and there was little difference in prevalence across ethnic groups.

## L. Risk factors

Alongside risk factors such as age, gender, genetics and socioeconomic determinants, lifestyle choices and related behaviours play a very significant role in the development of CVD by facilitating metabolic and physiological changes, thereby promoting atherosclerosis. Factors that are considered 'modifiable' through medical intervention, education and behavioural change at an individual level are indicated in Box 2.

**Time out activity 3**

Take some time to consider the bigger picture. What might be some of the other possible determinants of increased CVD risk at a macro level? Then visit the website to access the WHO Global Atlas on Cardiovascular Disease Prevention and Control [1] and read the short sections 17 and 18.

The WHO [1] states that the leading cardiovascular risk factor globally is hypertension, followed by cigarette smoking, glucose-related disorders, physical inactivity and being overweight or obese. Such behavioural and metabolic risk factors often co-exist in individuals and act together to increase the person's total risk of developing acute CVD-related episodes such as MI and CVA.

**Box 2. Risk factors in the development of CVD**

- Hypertension†
- Smoking†
- Dyslipidaemia†
- Family history of CVD
- Ethnic background
- Male gender
- Physical inactivity†
- Chronic renal disease [29]
- Older age
- Being overweight/obese especially truncal adiposity†
- Abnormalities in glucose tolerance, including diabetes mellitus and hyperinsulinemia†
- Episodic heavy alcohol consumption† [30]
- Chronic psychosocial stress† [31]
- Socioeconomic factors

† Factors considered 'modifiable' through medical intervention, education and behavioural change at an individual level.

Source: WHO 2011 [1] unless otherwise indicated.

The mechanism by which stress enhances risk of CVD had not been explained until recently. A study in the *Lancet* revealed that heightened activity in the amygdala was linked to an increased risk of CVD [31]. The amygdala is an area of the brain located within the temporal lobes that is involved in the processing of emotions and motivations, particularly those related to survival. Heightened activity in this area of the brain was linked to increased bone marrow activity, resulting in atherosclerosis and inflammation in the arteries.

The meta-analysis cited in the European guidelines on cardiovascular disease prevention in clinical practice reports on a number of psychological risk factors [32]. Mental health stressors mentioned include exposure to any life event that results in acute, strong negative emotions as well as personality traits that enhance such emotive reactions. The guidelines also cite chronic stress at work as a predictor of premature CVD-related health events. In addition, long-term stressful conditions in family life increase risk. Research has shown that clinical depression and depressive symptoms predict MI and CVA, and worsen subsequent prognosis. Anxiety is also an independent risk factor for cardiac events [33].

## M. Modifiable risk factors in people living with HIV

An overview of the research looking at risk-factor prevalence in PLWH reports significantly higher rates of diabetes, other glucose disorders, hyperlipidaemia and current smoking than exist in the general population [34]. Section J outlined the contribution of ART to these metabolic factors, but notably between 40% and 70% of PLWH smoke: a two- to three-fold increase from that of the general population. The contribution of smoking to the risk of CVD in PLWH is therefore considerable, and for many individuals this is the single most significant of all the known modifiable risk factors [26].

**Time out activity 4**

A good understanding of dyslipidaemia, including the significance of LDL and HDL cholesterol ratios and triglycerides, will assist you in identifying those at risk of CVD and in delivering patient education. A published supplement from the Joint British Societies makes consensus recommendations for the prevention of CVD.

Go to: http://heart.bmj.com/content/100/Suppl_2/ii1

Read section 2.1.13 for a summary of the key aims in relation to lipid profile for those at high risk for CVD.

**Key point**

Importantly, in relation to lipids, enhanced CVD risk is associated with elevated LDL and total cholesterol, low HDL cholesterol and elevated serum triglycerides.

Dyslipidaemia is an important risk factor and occurs in a high proportion of people with HIV infection. Furthermore, the pattern of disordered blood fats does not mirror that seen in the general population. Again, in the MACS study cohort [27], HIV infection was found to be associated with reductions in total cholesterol and both HDL and LDL-cholesterol. Those who commenced ART showed elevated total cholesterol and LDL-cholesterol but persistently reduced HDL cholesterol.

In addition, during a 10-year observation period, the D:A:D study found a substantial difference, with regard to raised triglyceride and total cholesterol levels between people taking ART and those who were yet to take treatment, as cited in Hemkens and Bucher's systematic review of the literature [23]. Interestingly, although more PLWH are treated with lipid and antihypertensive medication than in the general population, this study indicated that only modest decreases in lipids and blood pressure were achieved over time in this cohort.

The risk of lipid disorders is likely to be further enhanced by the increasing duration that people are taking ART. The independent effect of ageing on dyslipidaemia is also confounded by the direct effect of ART (as discussed in section J) and other CVD risk factors in the HIV-positive population; as well as by increases in the use of lipid-lowering medications in recent years. To further complicate the picture, the pattern of ART-related dyslipidaemia seen in those with pre-existing metabolic toxicities may differ from that seen in those who are new to treatment.

## N. Disease prevention

In the general population it is estimated that 90% of CVD is preventable [35]. There is strong, well-recognised scientific evidence that demonstrates reducing total cardiovascular risk, through interventions that address behavioural and metabolic risk factors, results in the prevention of MI and cerebrovascular accidents [1].

**Time out activity 5**

Consider what you know about the range of population-wide strategies in existence? To what extent have these influenced you, both as a lay-person and as a healthcare professional?

In the UK there are several population-wide strategies seeking to reduce incidence of CVD. These include a National Service Framework [36] and best practice guidance in the form of the Outcome Strategy for CVD from the Department of Health [37]. The work of charities such as the British Heart Foundation and Heart UK reinforces these strategies and seeks to identify those at risk early and certainly prior to a CVD-related episode, and to address modifiable risk factors. The National Institute for Health and Care Excellence

**Box 3. Summary of foundations for CVD prevention**

- A whole population, evidence-based, multi-faceted, integrated and policy-driven approach is required.
- Community engagement is important.
- A lifetime approach to risk reduction is most appropriate since both CVD risk and prevention are dynamic and continuous as people age and/or accumulate co-morbidities.
- Need to identify and target high-risk and hard-to-reach groups, alongside reinforcing key messages in relation to CV health to the whole population.
- Investment in addressing the full range of socio-economic factors that determine health inequalities is important to help narrow regional disparities.
- Establish robust local pathways for access to evidence-based smoking cessation and weight-loss programmes to reduce obesity.
- Promoting an increase in physical activity population-wide e.g. in schools and the workplace.
- In primary care: for people without diagnosed CVD but with a risk greater than 30% over 10 years, provide information about all modifiable risk factors and personalised advice about how they can be reduced.
- For the above risk group: medical intervention is advised to maintain blood pressure <140/85 mmHg, plus low-dose aspirin, statins and dietary advice to improve lipid profile.
- Consider insulin-sensitising and glucose-lowering pharmacological interventions (definitive supporting data for this is not yet robust).

**Key point**

The higher rates of CVD in PLWH may be linked in part to immune dysregulation even in the presence of effective HIV treatment and HIV medication; however, the main driver is almost certainly lifestyle and other factors including family history.

**Time out activity 6**

The European guidelines on cardiovascular disease prevention in clinical practice offer very specific targets for CVD prevention [32]. Download the pdf from https://academic.oup.com/eurheartj/article/37/29/2315/1748952/2016-European-Guidelines-on-cardiovascular-disease#35979598 and study the risk factor targets in Section 2.3.8, Table 6.

(NICE) has also produced comprehensive guidance on CVD risk assessment and management [29].

A summary of points reflecting a consensus, in terms of the foundations for effective CVD prevention, from the above strategies, is contained in Box 3.

Currently, there are few strategies or specific guidelines in place in relation to prevention of CVD in PLWH, beyond tailoring HIV therapy to avoid the drugs associated with CVD in patients with CVD or who are at high risk of CVD. We know, as mentioned previously, that smoking rates are disproportionately high in the HIV-positive population, therefore, reduction in smoking in these individuals is a health priority.

In terms of interventions to reduce modifiable risk factors, lifestyle changes are considered the first-line approach and there is good evidence that these are successful. A study by Shahmanesh *et al.* showed that over half of the European cohort who were at risk for cardiovascular disease were able to successfully modify that risk [38]. Almost one-third of smokers stopped smoking, and 25% of overweight people reduced their body mass index to <25 Kg/$m^2$ [38]. In terms of medical interventions, more than 50% of study participants with hypertension lowered their blood pressure but lipid-lowering treatment was less successful. Calvo-Sanchez and Martinez reviewed the evidence in terms of how to address smoking cessation in PLWH [39]. Box 4 summarises the key findings.

To date, there is little or no evidence to suggest that PLWH need to be offered more aggressive interventions to reduce modifiable risk factors than

**Box 4. Factors that facilitate smoking cessation**

- Routine and regular assessment of tobacco use
- Systematic and intensive counselling with follow up
- Routine unambiguous statements about the need to stop smoking
- Use of nicotine replacement formulations, e.g. patch, gum, sprays, alongside health advice
- Referral to specialist smoking cessation clinics
- Brief reminders regarding the benefits of nicotine abstinence
- Intervention by HIV clinic professionals – PLWHIV are better predisposed to consider medical advice given by HIV professionals
- Consider using information technology in support, e.g. text reminders
- Hypnotherapy and acupuncture
- e-cigarettes can reduce consumption of tobacco but to date the evidence is lacking

those used in the general population [26]; however, the British HIV Association (BHIVA) states that although firm evidence in HIV populations is lacking, the NICE guidelines are largely relevant and are endorsed [40]. As per the BHIVA guidelines, people with established CVD should be educated and supported to restrict dietary salt and saturated fat, reduce their alcohol intake and receive statins. For all PLWH, as with the general population, it is also advised to maintain a body mass index of 20–25 $Kg/m^2$ and increase physical activity. Stopping smoking is a health priority for this cohort given what we know of the disproportionately high numbers of smokers in this population.

In addition, switching to ART regimens that are not considered to be associated with dyslipidaemia, glucose abnormalities and/or other metabolic disturbances, alongside the continued maintenance of viral suppression is likely to be beneficial, especially in those assessed to be at high CVD risk (but only where there is minimal risk of treatment failure) [41]. Of note, a number of these interventions have a cumulative effect in reducing overall CVD risk.

**Time out activity 7**

Read further information on favourable treatment options and the rationale behind the above recommendations. Visit the BHIVA website and look at the Treatment Guidelines [41] section 8.6; available at: www.bhiva.org/documents/Guidelines/Treatment/2016/treatment-guidelines-2016-interim-update.pdf.

## O. Screening for risk and disease

Traditional and established CVD risk-assessment tools, while validated for use in the general population, have been found to underestimate the risk for PLWH. They do not take into account HIV-related factors likely to contribute to chronic inflammation or immune activation. The Cardiovascular Disease Prevention Pathway published by NICE [42] emphasises that when using risk calculators to inform drug-treatment decisions, other factors that may predispose the person to premature cardiovascular disease and which may not be included in the tool, must be taken into account. NICE also stresses that scores will underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These groups include people with inflammatory and autoimmune conditions, those with serious mental health problems, people taking certain medications such as steroids and PLWH. It is also important to recognise that risk will be underestimated in people who are already taking antihypertensive or lipid modification therapy, or who have recently stopped smoking. Use of clinical judgment is essential.

**Box 5. Commonly used risk-scoring systems**

- Framingham Risk Score for coronary heart disease
- Modified Framingham risk score
- D:A:D Cardiovascular Risk Equation
- Atherosclerotic cardiovascular disease (ASCVD) risk estimator
- QRISK2
- Joint British Societies for the prevention of cardiovascular disease Risk Calculator (JBS3)
- the SCORE tool
- The Prospective Cardiovascular Munster Study (PROCAM Health Check)

Six commonly used risk-scoring systems are listed in Box 5.

Of those listed above, only the D:A:D equation [43] was specifically developed for use with an HIV-positive population, as such it is the only one that attempts to take antiretroviral use into account. However, it does not consider key HIV-specific values such as CD4 cell counts and HIV viral load, and in fact performs similarly to the other tools in respect of its underestimation of risk in PLWH. The tools differ in the extent to which they incorporate several variables, for example racial and socio-economic factors and individuals' use of anti-hypertensive medication.

In a presentation at the 2014 Conference on Retroviruses and Opportunistic Infections, the first four tools listed in Box 5 were compared. The ASCVD's risk score had statistically significant superiority, in terms of accuracy, over the other three scores studied. The presenter concluded that although the risk-assessment tools have considerable overlap in their assessment methods, they differ, both in the cardiovascular events that they attempt to predict and in the variables that they consider. This clearly makes comparison challenging [44].

Of note, the risk calculation tool recommended by NICE is QRISK2 [29]. QRISK2 includes measures of ethnicity and considers socio-economic disparity. BHIVA guidelines suggest multiplying the score by 1.6 to adjust for HIV as a risk factor. BHIVA recommends baseline assessment of cardiovascular risk for those who are aged over 40 years and/or have significant CVD risk factors using the QRISK2 tool, but taking into account that it will underestimate risk, as mentioned earlier [41]. In terms of routine screening in an HIV clinic setting, BHIVA also makes several recommendations for annual investigations, depending on age, CD4, BMI etc (Box 6).

In addition, given what we know about the risk factors listed in Box 2, it is also important to assess alcohol consumption and to consider mental health (in particular, patients' experiences of stress), socio-economic factors such as poverty, social isolation, motherhood, employment status, working conditions and language limitations; all of which can impact

**Box 6. Summary of guidelines for monitoring CVD health in PLWH as per BHIVA recommendations [40,41]**

| Recommended monitoring/screening | Rationale |
|---|---|
| Use QRISK2 tool and multiply score by 1.6 to adjust for HIV | A score risk of >10% may require intervention/management |
| Check blood pressure annually | BP>140/90 increases risk of CVD and requires intervention |
| Review blood lipid profile annually | Lipid lowering interventions can reduce CVD risk |
| Check weight and calculate BMI annually | Obesity increases CVD risk and requires intervention to facilitate lifestyle modification |
| For smokers – advocate smoking cessation | Stopping smoking is critical to reducing CVD risk |

on the individual's ability to take up opportunities for diet and lifestyle modification. Individuals of low socio-economic status, older age or with mental health problems may need tailored programmes to meet their specific needs regarding information and motivational support.

## P. The role of the nurse in CVD risk reduction

Working alongside a multidisciplinary team, nurses are ideally placed and have the appropriate skill set to assess for CVD risk and to offer a number of interventions to support reduction in risk. Combining the knowledge and skills of the multidisciplinary team (composed of, for example, dieticians, psychologists, nurses and physiotherapists) into multimodal behavioural interventions can optimise preventive efforts and are especially recommended for individuals at very high risk [32].

There is considerable opportunity for nurses to use and further develop their skills in supporting lifestyle modifications. The use of motivational interviewing, a working knowledge of the holistic approach 'Process of Change' [45], together with the advanced communication skills used in other aspects of the nurses' role, such as treatment adherence support, are all very transferable techniques. Through the experience of providing treatment adherence support, for example, HIV nurses have learnt that previous unsuccessful attempts often affect self-efficacy for future behavioural change; and that the need to work in partnership, setting individualised and realistic goals is crucial to long-term success.

Unsurprisingly, mechanisms that link psychosocial factors to increased CVD risk include the increased likelihood of unhealthy lifestyle choices, for example, more frequent smoking, unhealthy food choices and less physical activity, as well as reduced adherence to behaviour change recommendations or risk-reducing medications. So, further opportunities for nurses evidently lie in the detailed assessment of psychosocial risk factors which we know have the potential to increase CVD risk (as discussed in depth in Section L).

Empowerment models of care, such as those routinely used in HIV today should also go a considerable way to facilitating behaviour change. An educative-supportive approach with individualised and holistic assessment is beneficial and forms a good basis for motivation and commitment. Building a therapeutic relationship over time and offering a combination of strategies is important for maximising opportunities for success.

**Time out activity 8**

Consider the relevance and value of assessment of psychosocial factors in your patients as this could well be an important element in decision making, especially in people who have been scored as near to interventional threshold. In addition, an understanding of the patients' psychosocial factors can help identify possible barriers to lifestyle changes. There are a range of standardised methods available to assess psychosocial influences on health. The Nominet Trust website lists several tools [46].

Have a look at: http://www.nominettrust.org.uk/knowledge-centre/evaluating-your-project/evidence-based-measurement-tools.

Then discuss with a colleague and/or your HIV MDT the potential benefit and applicability of using a tool for the assessment of psychological risk factors as routine practice in your clinic, area or region with a colleague and/or your MDT.

## Q. Conclusion

As advances in ART extend the lifespan of PLWH, it is likely that morbidity and mortality from cardiovascular disease will increase. Research findings give us considerable information on which to base social, educational and healthcare interventions, and the evidence base for the clinical management of CVD risk and disease in PLWH is expanding apace. Working in the field of HIV, as part of a holistic approach to care that seeks to enhance both quality, and quantity in terms of life expectancy, it is vital for nurses to contribute to the identification of those at risk. Nurses can also play a substantial role in supporting those individuals to tackle modifiable risk factors, working with the multidisciplinary team in the delivery of evidence-based clinical interventions and in influencing related policy and practice development.

**Time out activity 9**

Having read this article and completed the activities, for revalidation it is suggested that you now write a reflective account of your learning.

## R. Useful resources

Heart UK website. Available at: https://heartuk.org.uk

Joint British Societies (JBS2) guidelines on prevention of cardiovascular disease in clinical practice. *Heart*, 2005, **91 (Suppl 5)**, v1–v52.

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