

Screening for cardiovascular disease risk in people living with HIV

People living with HIV have a 1.5- to 2-fold increased risk of developing cardiovascular disease (CVD) compared to the general population, beyond what can be explained by traditional risk factors.¹

Traditional CVD risk calculators are known to underestimate risk in people living with HIV. However, Australian HIV guidelines still recommend the use of Australian CVD risk calculators in this patient population, but acknowledge that results are likely to underestimate risk.¹ Australian HIV guidelines recommend annual assessment of CVD risk factors in people living with HIV; this should include consideration of both traditional and HIV-specific risk factors.¹

Pharmacists can screen for risk factors for CVD in patients living with HIV and educate and refer those individuals at increased risk to see their doctor for a comprehensive clinical assessment.

Use this checklist to support your CVD risk screening in patients living with HIV

Step 1: Identify patients to screen

Pharmacists should consider screening every patient presenting on treatment with an antiretroviral medicine. If a patient is already under the care of a cardiologist, or their GP has recently reviewed their CVD risk; screening may not be required.

Consider:

Has your patient seen their GP about their CVD health in the past 12 months?	If answer is no to any of these	Screen for CVD risk. <i>Consider undertaking screening as part of a MedsCheck consultation if the patient is eligible</i>
Are they under the care of a cardiologist?		
Has your patient been prescribed lipid and/or blood pressure lowering medicine within the past 12 months?		



Supported by an unrestricted educational grant from Gilead

Step 2: Gather patient information

Record information about your patient using the table below. The Appendix contains an explanation of the increased risk.

Recognised risk factors

Evidence has shown people living with HIV have increased traditional CVD risk factors.^{1,3,4}

Patient details		
Age		
Sex at birth		
Ethnicity		
Family history of CVD	YES	NO
Medical history		
Existing CVD	YES	NO
Diabetes	YES	NO
Chronic kidney disease	YES	NO
Atrial fibrillation	YES	NO
Mental health condition		
Pharmacy based investigations		
Blood pressure, mmHg		
Total cholesterol (if available), mmol/L		
BMI		
Waist circumference, cm		
Lifestyle		
Current smoker (or quit in last 12 months)	YES	NO
Diet (portions of fruit and vegetables each day)		
Alcohol intake (standard drinks per week)		
Physical activity (exercise for 30+ minutes on how many days per week)		
Recreational drug use		

Reference: National Vascular Disease Prevention Alliance. Guidelines 2012²

HIV-related risk factors

Evidence suggests HIV-related risk factors may further increase CVD risk in people living with HIV.^{3,4,5}

HIV infection	
Most recent CD4 count	
HIV RNA level (viral load)	
Antiretroviral therapy	
Duration of treatment	
Prescribed antiretroviral therapy <i>(Antiretroviral medicines carry different levels of CVD risk and some have been shown to cause dyslipidaemia or weight gain)</i>	
Adherence to prescribed regimen <i>(How many doses are missed per week? Any recent cessation or interruption to therapy?)</i>	

Step 3: Assess risk and counsel patient

CVD in people living with HIV is the result of complex interactions between traditional risk factors, antiretroviral therapy and the chronic inflammation and immune activation associated with long-term HIV infection.² It is unknown to what extent each of these factors contribute.

Consider the information gathered in the previous section to help assess risk. Whilst HIV-specific CVD risk calculators are not recommended for use in Australia, this continues to be an active area of investigation.

Addressing modifiable CVD risk factors is still a priority; you can help your patient to reduce their risk through education and referral, if appropriate.

Counsel your patient about their risk factors based on the information you have gathered and support your patient to make positive lifestyle changes by offering counselling and advice. The following table contains suitable goals for patients to aim towards and reputable sources of information that can be used to aid discussion. If screening as part of a *MedsCheck* consultation, include any goals in a *MedsCheck* action plan. To ensure continuity of patient care, a copy of the action plan should be provided to the patient's prescriber. *Guidelines for pharmacists providing MedsCheck and Diabetes MedsCheck services* can be accessed on the PSA website.

Risk factor	Personal goal	General goal	Supporting resources
Smoking		Quit smoking and/or avoid second-hand smoke.	Quitline 13 7848 www.quit.org.au <i>Australian Pharmaceutical Formulary</i> non-prescription medicine guide—smoking cessation
Diet		Eat a heart-healthy diet rich in vegetables, fruits and wholegrains. Choose lean meats and, if you have high cholesterol, low fat dairy.	Heart Foundation recipes www.heartfoundation.org.au/search/recipes
Physical activity		Aim for 30 minutes of moderate-intensity physical activity on most days of the week.	Heart Foundation <i>Personal Walking Plans</i> : www.heartfoundation.org.au/personal-walking-plans
Alcohol		Drink no more than 10 standard alcoholic drinks per week and no more than four on any one day.	NHMRC <i>Alcohol Guidelines</i> www.nhmrc.gov.au/health-advice/alcohol
Weight		Aim for a waist measurement <80 cm for females or <94 cm for males.	Heart Foundation <i>Eating Well for a Healthy Weight</i> . Available at www.heartfoundation.org.au
Other			

Step 4: Refer patient

Patients are at high risk of an adverse cardiovascular event if they meet any of the following criteria²:

1. existing cardiovascular disease (coronary heart disease, stroke or peripheral vascular disease)
2. diabetes and age >60 years
3. a previous diagnosis of familial hypercholesterolaemia
4. systolic blood pressure ≥ 180 mmHg or diastolic blood pressure ≥ 110 mmHg
5. serum total cholesterol >7.5 mmol/L
6. Aboriginal and Torres Strait Islander adults aged over 74 years.

The *Australian Absolute CVD Risk Calculator* should be used during a complete clinical risk assessment conducted by a GP.⁶ Traditional CVD risk calculators are known to underestimate risk in people living with HIV. Australian HIV guidelines still recommend use of Australian CVD risk calculators in this patient population, but acknowledge that results are likely to underestimate risk.

Refer to Table 2—*Specific antiretroviral medicines and CVD considerations* and consider the patient's ART regimen when assessing overall CVD risk. Abacavir should be used with caution or avoided in patients with known high CVD risk. Higher cardiovascular risk has been reported in participants taking Darunavir-based regimens.

Refer your patient to their GP for a *Comprehensive heart health assessment* if they meet any of the high risk criteria. If CVD risk screening was part of a *MedsCheck* consultation, develop an action plan and provide this to the patient's prescriber.

References

1. Australian Society for HIV Viral Hepatitis and Sexual Health Medicine (ASHM). HIV Management in Australasia: a guide for clinical care. Darlinghurst: ASHM; 2019. At: <https://hivmanagement.ashm.org.au/>
2. National Vascular Disease Prevention Alliance. Guidelines for the management of absolute cardiovascular disease risk. Melbourne: Stroke Foundation; 2012. At: https://irp.cdn-website.com/5a7b1d9a/files/uploaded/Absolute_CVD_Risk_Full_Guidelines.pdf
3. Grand M, Bia D, Diaz A. Cardiovascular risk assessment in people living with HIV: a systematic review and meta-analysis of real-life data. *Curr HIV Res* 2020;18(1):5–18.
4. Currier JS. Epidemiology of cardiovascular disease and risk factors in patients with HIV. In: UpToDate. Waltham: UpToDate Inc; 2021. At: www.uptodate.com
5. ClinicalInfo. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. 2021. At: <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines>
6. Australian Chronic Disease Prevention Alliance. Australian absolute cardiovascular disease risk calculator. 2021. At: <https://www.cvdcheck.org.au/calculator>

Screening for cardiovascular disease risk in people living with HIV — Appendix

Background

Antiretroviral therapy (ART) has led to dramatic improvements in life expectancy for people living with HIV.¹

With an ageing population, 'traditional' or age-related risk factors for developing cardiovascular disease (CVD) are likely to become an increasing health issue for people living with HIV. This is in addition to risk associated with HIV infection itself.¹

CVD in people living with HIV is the result of complex interactions between traditional risk factors, ART-mediated side effects and the chronic inflammation and immune activation associated with long-term HIV infection.²

People with HIV infection have a higher plaque burden, particularly a greater burden of non-calcified (or 'vulnerable') plaque which has been shown to correlate with a higher risk of rupture and acute coronary events.³

People with HIV are also more likely to present with a ST-elevation acute myocardial infarction rather than a non-ST-elevation infarction or angina.⁴

Overall, it is important that health professionals and people living with HIV are aware of their increased risk of developing CVD and take actions to lower their risk.

Australian clinical guidelines for the management of HIV advocate for the assessment and management of traditional CVD risk factors in people living with HIV on an annual basis as per standard guidelines.²

Recognised risk factors

A recent systematic review and meta-analysis of real-life data of cardiovascular assessment in people living with HIV demonstrated that the most prevalent concomitant cardiovascular risk factors were dyslipidaemia (39.5%), smoking (33%), high blood pressure (19.8%) and diabetes (7.24%).⁵

Patient details	
Age	Patients living with HIV are at risk of premature onset CVD. ^{4,6}
Sex at birth	There may be a disproportionately higher risk of CVD in people living with HIV who were born female compared to those born male, however, there is currently insufficient evidence to address this relationship.
Ethnicity	People of Aboriginal, Torres Strait Islander, South Asian, Maori, Pacific Islander and Middle Eastern descent may have a higher CVD risk than estimated when using CVD risk calculators. ⁷
Family history of CVD	A family history of premature CVD increases individual risk of CVD, independent of traditional risk factors. A family history of premature CVD is coronary heart disease, stroke or peripheral vascular disease in relatives including parents, grandparents, uncles and/or aunts before the age of 55 years. ⁷
Medical history	
Existing CVD	Existing coronary heart disease, stroke or peripheral vascular disease increases your risk of future cardiovascular events. ⁷
Diabetes	People with type 2 diabetes have a twofold increased risk for CVD. ⁷
Chronic kidney disease (CKD)	People with moderate or severe CKD (defined as persistent proteinuria or eGFR <45 mL/min/1.73m ²) have an increased risk of developing CVD. The prevalence of CKD in HIV-infected adults exceed those of the general population. ⁸
Atrial fibrillation	Atrial fibrillation is an important marker of thromboembolic disease, stroke and incident all-cause mortality, cardiovascular death, heart failure and possibly coronary events. ⁷
Mental illness	Clinical depression, social isolation and lack of quality social support are risk factors for CVD and have been shown to worsen CVD prognosis. ⁷

Investigations	
Blood pressure, mmHg	- Hypertension is common in people living with HIV but has been linked to well-known risk factors such as age, sex and BMI.⁶ However, it is difficult to determine the contribution of ART, chronic inflammation caused by HIV and traditional risk factors on hypertension risk. - Australian HIV guidelines recommend treating hypertension in line with currently available guidelines.²
Total cholesterol (if available), mmol/L	- Dyslipidaemias are highly prevalent in people living with HIV (with and without ART) and contribute to increased CVD risk. The reasons why HIV infection causes a shift in lipid profile are not yet understood.^{2,6} - People living with HIV tend to have low HDL cholesterol and elevated triglycerides. Lower levels of HDL cholesterol in people living with HIV has also been associated with increased CVD risk.^{2,6} - Initiation of ART leads to further increases in triglycerides, along with increases in total cholesterol and LDL cholesterol.^{2,6} - The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study of over 23,000 HIV patients showed a higher rate of total cholesterol and triglycerides associated with increased incidence of myocardial infarction.⁹ - Refer to Table 1—Patient CVD risk factors and antiretroviral therapy considerations and Table 2—Commonly-prescribed antiretroviral medicines and CVD considerations for ART effects on lipids.
BMI and waist circumference	- Individuals with a BMI ≥ 25 kg/m² are classified as overweight and those with a BMI ≥ 30 kg/m² are obese and at increased risk of CVD compared with individuals with normal BMI. Aim for a waist measurement <80 cm for females or <94 cm for males.⁷ - Refer to Table 1—Patient CVD risk factors and antiretroviral therapy considerations and Table 2—Commonly-prescribed antiretroviral medicines and CVD considerations for ART effects on weight gain.
Lifestyle	
Current smoker (or quit in last 12 months)	- Over one third of people with HIV in Australia are smokers, which is more than twice the rate of the general Australian population.⁴ - CVD risk in people living with HIV decreases significantly with each year of having quit smoking, after three years of quitting their risk of CVD halves compared to the first year.⁴ - Australians living with HIV were more likely to quit at the time of HIV diagnosis or ART initiation, therefore these are opportunities for successful smoking cessation interventions.⁴
Diet	- Poor diet is a risk factor for CVD. - A diet rich in vegetables, fruit, wholegrains and healthy fats reduces CVD risk. The Heart Foundation also recommends reducing salt intake and, for people with high cholesterol, choosing low fat dairy options.
Alcohol intake	- There is growing evidence that any alcohol increases CVD risk, despite previous evidence showing low-level consumption being cardioprotective. - The Heart Foundation currently advises that people should drink no more than 10 standard alcoholic drinks per week and no more than 4 on any one day.
Physical activity	30 minutes of moderate-intensity physical activity on most days of the week can help reduce CVD risk.
Recreational drug use	Recreational drugs (such as cocaine, ecstasy, and amphetamine) can have cardiovascular effects, ranging from abnormal heart rate to increased risk of heart attacks. Cocaine and marijuana use has been associated with CVD risk in people living with HIV.

HIV-related risk factors

HIV infection	
CD4 count	People with recent or prior CD4 counts of <500 cells/mm ³ are at increased risk of CVD. ⁶
HIV RNA levels	People with a detectable HIV RNA level (often defined as a viral load of >50 RNA copies/mL) have a higher CVD risk. However, ongoing inflammation due to chronic infection persists despite undetectable HIV RNA levels. ⁶
HIV medicines	
Antiretroviral therapy is associated with lower mortality but increased CVD risk. ^{3,6} Some antiretroviral medicines used to treat HIV infection have been associated with an increased risk of cardiovascular disease, whilst other medicines have been shown to cause dyslipidaemia. In addition, some of the newer medicines have now been associated with weight gain. ^{2,6}	
Duration of treatment	- Longer duration of antiretroviral therapy is associated with an increased risk of CVD. This may be related to both the current and previous antiretroviral regimens received. - Protease inhibitors have been shown to increase risk of CVD, and this risk increases over duration of therapy. - Cumulative use of ritonavir-boosted darunavir has been associated with a progressively increasing risk of CVD over 5 years.⁹
Prescribed antiretroviral therapy	- Antiretroviral medicines carry different levels of CVD risk. - Refer to <i>Table 1— Patient CVD risk factors and antiretroviral therapy considerations</i> and <i>Table 2— Commonly-prescribed antiretroviral medicines and CVD considerations</i> for ART effects on CVD risk.
Adherence to prescribed regimen	Cessation, interruption or failure to take prescribed antiretroviral therapy can further increase risk. ^{2,6}

Table 1 Patient CVD risk factors and antiretroviral therapy considerations

Patient factors	Medicines implicated	Evidence	Consideration
Established high CVD risk	Abacavir	Increased risk of cardiovascular events observed in some studies.	Use with caution or avoid in patients with known high CVD risk.
	Boosted HIV-protease inhibitors: Darunavir + ritonavir Fosamprenavir + ritonavir Lopinavir + ritonavir	Increased risk of cardiovascular events observed observational cohort studies.	Use with caution or avoid in patients with known high CVD risk.
	Certain antiretroviral regimens associated with more favourable lipid profiles	Evidence on whether using antiretroviral regimens with more favourable lipid profiles improves cardiovascular outcomes is lacking.	Consider switching antiretroviral regimens in some cases.
Hyperlipidaemia	Protease inhibitor* + ritonavir or protease inhibitor + cobicistat	Known to increase blood lipids.	Fewer lipid effects with regimens containing: - bictegravir - dolutegravir - raltegravir - rilpivirine
	Efavirenz	Known to increase blood lipids.	
	Elvitegravir + cobicistat	Known to increase blood lipids.	
	Tenofovir disoproxil fumarate	Known to lower blood lipids.	Switching from tenofovir disoproxil fumarate to tenofovir alafenamide associated with increased lipids.
Weight gain	- bictegravir - dolutegravir - elvitegravir + cobicistat - raltegravir	Known to cause weight gain. Greatest weight gain seen with bictegravir and dolutegravir.	Effect greater with integrase strand transfer inhibitors than other antiretroviral drug classes.
	Tenofovir alafenamide	Reported to cause weight gain, though other studies have found it to be weight neutral.	Greater weight increase with tenofovir alafenamide than tenofovir disoproxil fumarate. Greater weight gain with certain integrase strand transfer inhibitor regimens used in combination with tenofovir alafenamide. Unclear whether change of therapy results in reversal of weight gain.

*Protease inhibitors include atazanavir, darunavir, fosamprenavir, lopinavir, tipranavir.

Reference: Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV¹⁰, Currier JS¹¹

Table 2 Commonly-prescribed antiretroviral medicines and CVD considerations

Medicine	Adverse effects	Comments	General advice
Abacavir	Increase in cardiovascular events associated with abacavir use in some cohort studies.	Risk associated with recent (i.e., within 6 months) or current use of abacavir.	Absolute risk greatest in patients with traditional CVD risk factors. Use with caution or avoid in patients with known high CVD risk. Consider switching to an alternative in established CVD.
Tenofovir alafenamide	↑TG, ↑LDL, ↑ HDL (no change in TC:HDL ratio).	Tenofovir disoproxil fumarate lowers lipids, therefore lipids often increase when switching from tenofovir disoproxil fumarate to tenofovir alafenamide. Some studies have reported greater weight gain with tenofovir alafenamide than tenofovir disoproxil fumarate.	Clinical significance of dyslipidaemia is unclear.
Tenofovir disoproxil fumarate	Has been associated with weight loss	Lowers lipids. Associated with lower lipid levels than abacavir and tenofovir alafenamide.	Although potential lipid-lowering and weight loss effects, tenofovir disoproxil fumarate is rarely used in practice in Australia due to potential renal and bone toxicity.
Bictegravir	Weight gain	Has fewer lipid effects.	Clinical significance of weight gain is unclear.
Dolutegravir	Weight gain	Has fewer lipid effects.	Clinical significance of weight gain is unclear.
Elvitegravir + cobicistat	↑TG, ↑LDL, ↑ HDL Weight gain		Clinical significance of weight gain is unclear.
Raltegravir	Weight gain	Has fewer lipid effects.	Clinical significance of weight gain is unclear.
Efavirenz	↑TG, ↑LDL, ↑ HDL	Fewer lipid effects seen with alternative non-nucleoside reverse transcriptase inhibitor rilpivirine.	Efavirenz now used less frequently due to toxicity profile.
Atazanavir + ritonavir Atazanavir + cobicistat	↑TG, ↑LDL, ↑ HDL	Association between other protease inhibitors (darunavir, fosamprenavir and lopinavir) and cardiovascular risk not seen with atazanavir in some studies, though further study needed.	If a boosted protease inhibitor required, atazanavir may be preferred over other protease inhibitors.
Darunavir + ritonavir Darunavir + cobicistat	Associated with cardiovascular events in some cohorts. ↑TG, ↑LDL, ↑ HDL	Higher cardiovascular risk reported in participants taking darunavir-based regimens than in those taking atazanavir-based regimens in observational cohort study.	If a boosted protease inhibitor required, atazanavir may be preferred over darunavir. Protease inhibitors generally considered less favourable due to toxicity profile.

HDL = high density lipoprotein; LDL = low density lipoprotein; TG = triglycerides; TC = total cholesterol.

Reference: Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV¹⁰, Currier JS¹¹

References

- Samji H, Cescon A, Hogg RS, Modur SP, Althoff KN, Buchacz K, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. *PLoS One* 2013;8(12):e81355
- Australian Society for HIV Viral Hepatitis and Sexual Health Medicine (ASHM). HIV Management in Australasia: a guide for clinical care. Darlinghurst: ASHM; 2019. At: <https://hivmanagement.ashm.org.au/>
- Althoff KN, McGinnis KA, Wyatt CM, et al. Comparison of risk and age at diagnosis of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer in HIV-infected versus uninfected adults. *Clin Infect Dis* 2015;60(4):627–38.
- Lo J, Abbara S, Shturman L, Soni A, Wei J, Rocha-Filho JA, et al. Increased prevalence of subclinical coronary atherosclerosis detected by coronary computed tomography angiography in HIV-infected men. *AIDS* 2010;24(2):243–53.
- Grand M, Bia D, Diaz A. Cardiovascular risk assessment in people living with HIV: a systematic review and meta-analysis of real-Life data. *Curr HIV Res* 2020;18:5–18.
- Hejazi N, Huang MS, Lin KG, Choong LC. Hypertension among HIV-infected adults receiving highly active antiretroviral therapy (HAART) in Malaysia. *Glob J Health Sci* 2013;6(2):58–71.
- National Vascular Disease Prevention Alliance. Guidelines for the management of absolute cardiovascular disease risk. Melbourne: Stroke Foundation; 2012. At: https://irp.cdn-website.com/5a7b1d9a/files/uploaded/Absolute_CVD_Risk_Full_Guidelines.pdf
- Cheung J, Pühr R, Petoumenos K, Cooper DA, Woolley I, Gunathilake M, et al. Chronic kidney disease in Australian human immunodeficiency virus-infected patients: analysis of the Australian HIV Observational Database. *Nephrology (Carlton)* 2018;23(8):778–86.
- Ryom L, Lundgren JD, El-Sadr W, Reiss P, Kirk O, Law M, et al. Cardiovascular disease and use of contemporary protease inhibitors: the D:A:D international prospective multicohort study. *Lancet HIV* 2018 Jun;5(6):e291–300.
- ClinicalInfo. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. 2021. At: <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines>
- Currier JS. Epidemiology of cardiovascular disease and risk factors in patients with HIV. In: UpToDate. Waltham: UpToDate Inc; 2021. At: www.uptodate.com