Minimising the risk of cardiovascular disease (updated)

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This Treataware fact sheet explains the current knowledge about cardiovascular (heart) disease risk in people living with HIV/AIDS, and some strategies for minimising risk.

The full text of the fact sheet is below. You can also download a printable PDF copy [1] of this resource, or contact us [2] to obtain hard copies.

Introduction

Cardiovascular disease (CVD) refers to a group of diseases and illnesses of the heart and blood vessels. One of the most common of these diseases is coronary artery [3]One of the two arteries that supply the heart with oxygenated blood. disease, a narrowing of the arteries supplying blood to the heart, caused by deposits of fatty plaque [4]A sticky substance that forms on the surface of the teeth, helping bacteria growth and acid formation beneath its surface, and causing tooth decay. Plaque build-up can irritate the gums and cause gum disease. Removal of plaque through regular brushing and flossing is the key to good oral hygiene.. Blockage of these arteries can lead to angina [5]temporary chest pain or a sensation of pressure due to a lack of oxygen supply to the heart. Also called angina pectoris. (chest pains) or heart attack [6]A life-threatening emergency in which the blood supply to the heart is suddenly cut off, causing the heart muscle (myocardium) to die from lack of oxygen..

Over the past few years, reports of CVD have been increasing in otherwise healthy HIV positive men. Whether this perceived increased incidence is due to HIV infection itself, the antiretroviral drugs or the prevalence of traditional risk factors within this group is the subject of some debate. Although the majority of HIV positive people in Australia are male and receiving increasingly effective treatments, the risk of CVD increases with age. This applies to both sexes, as women tend to lose any protection from CVD once they become post-menopausal.

Many studies have been performed to identify factors that increase a person's risk for CVD. Two important studies are the Framingham Heart Study and Caerphilly Study. The Framingham Heart Study, a 50-year study which began in 1948, involving 10,000 people over two generations, is the most extensive study of cardiovascular risk factors yet undertaken in the general population. The Caerphilly Study is a 20-year study of cardiovascular disease in 3,000 men aged 45 to 59 years, recruited between 1979 and 1983, all of whom lived in the town of Caerphilly in Southern Wales (UK). From these studies we know that the following factors are associated with an increased risk of CVD:

- Male gender
- Older age (>45 for males and > 55 for females)
- Family history of cardiovascular disease
- Tobacco smoking (2.3 fold increased risk)
- Obesity
- Abdominal fat accumulation (gain of fat around the belly)
- High-fat diet
- Lack of exercise
- Serum lipid [7]A fat. abnormalities
- High total cholesterol [8]An essential component of cell membranes and nerve fibre insulation, cholesterol is important for the metabolism and transport of fatty acids and the production of hormones and Vitamin D. Cholesterol is manufactured by the liver, and is also present in certain foods. High blood cholesterol levels have been linked to heart disease and may be a side effect of some anti-HIV medications. (>5.2 mmol/L 1.5 fold increased risk)
- High low-density lipoprotein (LDL) cholesterol level
- Low high-density lipoprotein (HDL) cholesterol level (<1.0 mmol/L, 1.4 fold increased risk)
- High triglyceride [9]A type of fat in the blood. Elevated triglyceride levels may be a side effect of some anti-HIV drugs. level (>2.0 mmol/L, 1.8 fold increased risk)
- High blood pressure [10]Persistently high blood pressure, an outwardly symptomless condition which carries an increased risk of serious illnesses such as stroke, heart disease and heart attack. (hypertension) >140

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systolic and/or >90 diastolic (1.5 fold increased risk)
Impaired Glucose metabolism
Diabetes [11][Diabetes mellitus] A disorder in which sugars in the diet cannot be metabolised into energy due to a lack of the enzyme insulin. Late-onset diabetes mellitus may be a long-term side effect of some anti-HIV drugs. (fasting glucose >7 mmol/L, 2.3 fold increased risk)
High blood glucose level
Insulin resistance [12]A diabetes-like condition in which, while adequate amounts of insulin are produced by the pancreas, the body does not respond normally to the action of insulin. In the wider community, insulin is related to obesity, while in HIV it may be related to lipodystrophy.

These risk factors can be broadly classified into those that can be modified, such as stopping smoking, reducing high cholesterol and exercising more, and those that cannot be altered (non-modifiable factors) such as increasing age, gender and family history. All of these factors need to be taken into consideration when assessing a person's overall risk of CVD.

Studies have shown high prevalence of some of these risk factors in HIV positive people. The HIV Futures 4 study (www.latrobe.edu [13]. au/hiv-futures) conducted by the Australian Research Centre in Sex, Health and Society ([14]Australian Research Centre in Sex, Health and Society, part of La Trobe University in Melbourne. For further information see http://www.latrobe.edu.au/arcshs/ [15].) found that 48 percent of HIV positive people smoked, compared to 30 percent of the general population.

These factors, coupled with changes in cholesterol levels and increased diabetes seen in some positive people who are on long term antiretroviral treatment, could go some way to explain the increased incidence of CVD observed in some studies. However, the importance of each of these risk factors in the setting of HIV infection and its therapy is only beginning to emerge.

More light has been shed on this area by a large international study known as Data Collection of Adverse Events of Anti-HIV Drugs – or the 'DAD' study. This study is similar to the Framingham study, only it investigated risks for heart attack and other forms of CVD in people who were HIV positive. Almost 23,500 people from various centres all over the world were enrolled [16]The act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process., starting in 1999 with follow-up until 2002. More than 24% were female and, similar to the HIV Futures 4 study, 56.2% of the participants smoked. The first set of results, published in 2003, showed increased risk of heart attack in HIV positive people with traditional risk factors such as older age, being male or having a family history of heart disease. In addition, treatment with combination antiretrovirals [17]A medication or other substance which is active against retroviruses such as HIV. was also associated with an increased risk of heart attack, even when the other traditional risk factors (such as gender) were taken in to account. The risk of heart attack increased per year of combination antiretroviral treatment, with an increase of 26% per year of therapy during the first four to six years of treatment.

Although this may seem disturbing, the overall mortality rate in this study was 2% and the rate of death from heart attack was only 0.13%. When compared to a yearly mortality rate of 20% seen in positive people prior to combination antiretroviral therapy, there is still a clear health benefit from taking appropriate, effective treatment for HIV. These initial results could not determine if specific antiretroviral drugs were associated with this increased risk, but further follow-up is underway and future analyses may give more detailed insights into why HIV therapy may cause increases in heart attack and CVD.

There are three major ways in which people with HIV can potentially modify their risk factors for heart disease

Risks associated with chronic infection with HIV:

Chronic infection with HIV can lead to constant and ongoing inflammation in the body, which may increase the risk for CVD. Studies have also found that HIV positive people with detectable virus [18]A small infective organism which is incapable of reproducing outside a host cell. also have lower levels of the good cholesterol (HDL) in their blood. The higher the viral load [19]A measurement of the quantity of HIV RNA in the blood. Viral load blood test results are expressed as the number of copies (of HIV) per milliliter of blood plasma., the lower the HDL in the

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blood. Low HDL is associated with increased risk of CVD. By reducing the amount of HIV in the body, antiretroviral treatment can reduce inflammation and increase HDL in some people. However, there is no clinical [20]Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. evidence that this reduces risk for heart disease and, as discussed above, combination treatment itself also affects risk of CVD. Despite this, the risk-benefit ratio of treatment over no treatment clearly favours effective antiretroviral treatment when clinically indicated. Traditional cardiovascular risks are much more important to address than the risks associated with antiretroviral therapy with regards to CVD in HIV positive people.

Lifestyle issues

Smoking

Smokers have an overall 70% greater mortality rate than non-smokers. Most people are aware that smoking causes lung cancer, but as well as this, cardiovascular disease also claims the lives of many smokers. In Australia in 1998, the Australian Institute of Health and Welfare estimated there were 19,019 deaths attributed to smoking, including lung cancer, breathing disorders and cardiovascular disease.

Damage or disease of the heart, arteries, veins and smaller blood vessels can all be increased by smoking. Coronary artery disease (which can lead to heart attacks) is the largest single cause of death in men and women in Australia, causing 24% of all deaths. Strokes are also more common in smokers. Stroke occurs when artery disease affects the blood vessels supplying blood to the brain.

If blockage occurs and interrupts this blood supply, the brain can be damaged, which can affect muscle power, speech and other complex brain functions. When compounded with other risk factors associated with HIV and its treatment, smoking is the one single modifiable factor that is likely to contribute to the risk of arterial disease and CVD. For these reasons, besides taking effective antiretroviral treatment, quitting smoking is the single most positive step a person with HIV can take towards maintaining their health.

QUIT Programs

Quitting smoking can be a difficult task for many people, but the benefits to your health and quality of life are immeasurable. There is much to be gained from quitting: you'll improve your health and fitness, not to mention your finances.

Many of the State and Territory positive organisations and AIDS councils have QUIT Smoking Programs. Your local positive organisation or AIDS council will have the contact details for QUIT Programs in your area. If there is no specific QUIT program in your area, there are general programs run through many community-based health organisations. You may also choose to do it on your own. Regardless of your strategy, there are many aids to help you quit smoking, including nicotine replacement patches and gum. If you are considering quitting smoking, talk to your local doctor about the options available to you.

Hypertension (High Blood Pressure)

Many things can cause hypertension or high blood pressure in HIV+ people.

These include:

- HIV infection itself
- poor nutrition (especially high amounts of fat or salt)
- weight gain (especially abdominal fat gain)
- smoking
- drinking excessive alcohol
- family history of hypertension
- amphetamine use

People with HIV-associated lipodystrophy may be at increased risk of hypertension. Although the exact reasons why this happens are not known, lipodystrophy can cause changes in weight, such as gain in central fat (around

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the trunk and the belly) which may contribute to increases in blood pressure. Hypertension is another major contributor to long-term increased risk of CVD. Effective treatments are available and, if you are overweight, losing weight and taking moderate aerobic exercise may be enough to normalise the blood pressure. Should these simpler solutions fail to control hypertension, your doctor may recommend medications to lower blood pressure. If you have any of the above risk factors, you should have your doctor check your blood pressure regularly.

Obesity

Everyone's ideal body weight is different and depends on their gender and their height. To control for these differences, an index called the Body Mass Index (BMI) has been devised. To calculate your BMI, divide your body weight in kg by your height in meters squared [e.g. if you are 75kg and are 1.75M tall, your BMI is 25 (75 divided by 1.75 times 1.75)]. A normal BMI lies between 18.5 and 25.

High BMI, or obesity, is an important modifiable risk factor for hypertension. A BMI greater than 27 and a waist circumference greater than 90cm for females or 100cm for males are associated with increased risks of hypertension, dyslipidaemia, diabetes and CVD mortality. Weight reduction of as little as 4.5 kg has been shown to reduce blood pressure in a large percentage of overweight people with hypertension. This index applies to the general population, but may not, however, be as easily applicable to people with moderate/ severe lipodystrophy. If you are in doubt, talk to your doctor and/or dietician if you think you may be overweight.

Dietary considerations. While it is difficult to make generalised dietary recommendations for HIV positive people, in the context of reducing CVD risk, reduced consumption of saturated fats (found in meat, chicken skin, processed cakes and biscuits, butter, full-cream dairy products, and many ‘fast foods') is recommended and replaced where possible by monounsaturated and polyunsaturated fats (like olive oils and vegetable oils, including omega-3 fats found in fish oils).

Although some studies have found that alcohol may have a protective effect on risk of CVD, excess alcohol can be associated with hypertension and abdominal fat gain, both of which can increase the risk for CVD. Therefore, reducing alcohol intake to less than three standard drinks a day is desirable. Even if you are going on a diet to reduce weight, it is vital that you maintain good nutrition. Decisions regarding changes to your diet should be made in conjunction with a specialist HIV dietician, whenever possible.

Exercise

Regular exercise is of benefit to everyone's health, including people with HIV. It can have a positive effect on your immune system as well as lowering your stress levels, lowering your blood pressure and reducing your weight. However, some factors need to be taken into consideration before starting an exercise program.

First of all, discuss the exercise program with your doctor, dietician (if available) and trainer to customize the program. The following should be taken into account:

- the goals of the program
- a baseline [21]1. Information gathered at the beginning of a study from which variations found in the study are measured. 2. A known value or quantity with which an unknown is compared when measured or assessed. 3. The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment which is being tested. At this reference point, measurable values such as CD4 count are recorded. Safety and efficacy of a drug are often determined by monitoring changes from the baseline values. and ongoing monitoring mechanism to assess your progress
- clearly defined limits to the program to avoid “over-doing it”
- advice from an HIV specialist dietician regarding changes to your nutritional needs resulting from uptake of the exercise program.

Defining your Goals

Different people have different goals depending on their age, general health status, physical limitations and severity of HIV disease. Some people will want to obtain top physical condition while others will be satisfied to lose a little weight, increase mobility and lessen pain or discomfort.

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Energy Levels

People with HIV often complain about low energy levels. A sensible exercise program will increase energy levels, and fatigue can be avoided if consideration is given to your current fitness level as well as avoiding exercise when energy levels are at their lowest. It may be a good idea to exercise at those times of the day when you know that your energy levels will be at their highest.

Maintaining Muscle (or Lean Body) Mass and Healthy Bones

All exercise consumes energy, so it is important to include sufficient carbohydrates in your diet to support the additional energy expenditure. Not eating enough fuel such as complex carbohydrates, will lead to loss of muscle and other lean body mass as a substitute for fuel energy. Paying attention to sufficient calcium intake during an exercise program will also help maintain healthy bones.

In summary;

Regular exercise for people with HIV can:

- improve cardiovascular function and help control blood pressure
- decrease stress levels
- increase muscle mass and strength
- improve energy levels
- improve appetite
- help restore normal sleep patterns

Risks associated with HIV antiretroviral treatment

Alterations to glucose and fat (lipid) metabolism and changes in body fat distribution can occur with long-term treatment of HIV infection with combination antiretroviral therapy. Some of these changes may affect your risk of CVD.

Disorders of Fat (Lipid) Metabolism

As discussed above, even before the advent of combination antiretrovirals, HIV positive people were noted to have lower levels of HDL (good) cholesterol. When combination therapy [22]Highly Active AntiRetroviral Therapy ??? aggressive treatment of HIV infection using several different drugs together. was introduced in the mid-1990s, doctors and patients noticed increases in triglyceride (fatty acid) levels and levels of low-density lipoprotein or LDL cholesterol (bad cholesterol). The extent of changes differed from patient to patient and depending on the type of combination therapy used.

Both sexes experienced these changes with some studies reporting larger increases in HIV positive women and the changes were more frequently noted in patients prescribed combination therapy containing protease inhibitors (PI). How exactly the treatment causes these changes in lipid metabolism is still being investigated and the contribution of these changes in lipids to risk of CVD is still being evaluated. The DAD and subsequent studys have shown elevations in cholesterol and triglyceride levels didn't explain the increased risk of heart attack seen with exposure to combination antiretrovirals.

Several approaches have been used to lower the cholesterol and triglyceride levels in patients on therapy. Lifestyle changes, such as introduction of a low fat diet, weight reduction and increased physical exercise, although not proven in studies, may be helpful in reduction of overall risk of CVD. Switching drugs in the regimen to ones that are known not to cause lipid changes may also help in some individuals. Lipid-lowering medications can also be considered but studies have shown these medications to be less effective among people with HIV on antiretroviral therapy than in the general population.

Lipid-lowering drugs, called statins, have been shown to reduce total and LDL cholesterol levels in HIV positive patients, although they are less effective than in the general population. Atorvastatin and pravastatin are preferred

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as they interact less with antiretrovirals than other statins. Another class of lipid-lowering drugs called fibrates can be used to decrease triglyceride levels and when used with statins may have an additive effect. Examples of fibrates include gemfibrozil, fenofibrate and bezafibrate.

All the interventions described here carry risks . Switching antiretroviral drugs can introduce new side-effects and may not be as effective in keeping HIV under control, which can lead to treatment failure and, in some cases, development of viral resistance. Lipid-lowering drugs have their own side effects and have the potential to interact with antiretrovirals or other medications. In addition, HIV positive people have different dietary, nutritional and exercise requirements than the general population. As such, commonly used diets may not be recommended in your specific case. All of these issues need to be taken into account and any strategy to address lipid abnormalities should be introduced in conjunction with your HIV doctor and dietician. In particular, if it is recommended that you start a lipid-lowering medication, you should discuss it with the doctor who looks after your HIV before you start it.

Insulin resistance and diabetes

Normally blood glucose is distributed to your body's tissues under the control of insulin. Glucose is then used as a fuel to meet your body's energy requirements. In some cases, this process is disturbed and more insulin is needed for the tissues to take up glucose from the blood. The tissues are said to be more ‘resistant' to insulin and this leads to a condition called ‘insulin resistance' which can subsequently lead to diabetes, a condition in which blood glucose levels become quite high. In the general population, insulin resistance is becoming more common, especially in older people and those with high BMI and it is known to be associated with increased risk of CVD.

Before the advent of combination antiretroviral therapy, insulin resistance and diabetes were uncommon in people with HIV. Recent studies have shown that insulin resistance is more common in HIV positive people on treatment, especially in those with increased central fat, such as increased trunk fat and in those with “buffalo hump” (abnormal fat accumulation in the dorsocervical region between the shoulders). In the DAD study, HIV positive people with diabetes were more than twice as likely to have a heart attack than those without diabetes.

Many factors contribute to this increased insulin resistance, including direct effects of the drugs and indirect effects related to changes in body fat (especially increases in central fat). Monitoring fasting blood glucose levels before and during treatment with combination antiretrovirals can help identify problems with insulin resistance and diabetes. If diabetes is diagnosed, it should be treated in the same way as diabetes in the general population.

If you are diagnosed with diabetes, it is important that you are regularly monitored by a diabetes specialist (an endocrinologist) in conjunction with your HIV prescriber.

Body Fat Distribution Changes

Anti-HIV treatment, particularly some protease inhibitors and nucleoside reverse transcriptase inhibitors, have been associated with changes in body fat.

Together with the abnormalities in lipid and glucose metabolism, these fat changes have become known collectively as HIV- associated lipodystrophy (HIVLD). This syndrome is associated with a mixture of gain in central fat (around the belly and trunk) and loss of fat from the arms, legs and face (lipoatrophy). Although most affected people experience a mix of fat loss and fat gain, some people are affected predominantly by fat gain while others by predominantly fat loss. HIVLD is a complex syndrome, affects both men and women and many factors contribute to its development. There are no proven treatments for HIVLD, although many doctors now try to use safer combinations of antiretrovirals in order to prevent lipodystrophy occurring. As to whether or not HIVLD increases risk of CVD, the DAD study did not show a significant association between HIVLD and heart attack, although the authors acknowledged that longer follow-up in this study is needed before a definitive answer is known.

Finally, because treatments for HIV have improved dramatically over the past couple of years, and hopefully will continue to do so, many HIV positive people now have a close-to-normal life expectancy. Medication side effects are still a problem for many and CVD risk is increased. Nonetheless for these reasons, HIV positive people should seek support to renew their health attitudes and approaches with a longer-term goal in mind, which lessens these concerns. Unless CVD risk factors, such as the high rates of smoking, are seriously addressed by HIV positive

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people, many of the gains of successful HIV treatment in terms of longevity and wellbeing may be lost.

Attachment	Size	Type
PDF version of this fact sheet [23]	1.78 MB	PDF

- diabetes
- heart disease
- Lipodystrophy and lipoatrophy
- smoking
- Treataware
- Treataware fact sheets

Links:
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