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adherence

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Written by Michael Carter Fourth edition 2007

NAM is a charity that publishes information for people affected by HIV and those working with them. We believe information helps people to make decisions about, and be in control of, their lives, health and treatment options.

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adherence

Taking your medication properly (or adherence - the term that will be used throughout this booklet) is the most important factor under your control in the success of your anti-HIV treatment. This booklet explains why adherence is important and provides some hints on actions you could take to improve your adherence. A summary can be found on page 32 and a glossary of words used on page 33. This booklet is not intended to replace discussion with your doctor. However, it may help you to decide what questions to ask your doctor about any course of treatment you may be considering.

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1

What is adherence?

Adherence means sticking to, or being loyal to. Adherence to your HIV treatment regimen means taking your pills at the right time, in the right doses and in the right way.

Taking your HIV drugs properly involves the following:

- **Taking all the medicines which make up your combination in the right quantities.**
- **Taking your pills at the right times.**
Taking your medication at the wrong time can cause a rise in viral load and this may lead to the development of drug resistance.
- **Making sure you take your medication with or without food, according to instructions.**
Some medicines need to be taken with food to ensure that the body absorbs them properly but others need to be taken on an empty stomach, a certain amount of time before or after you eat. It can also be important that you eat the right kind of food - the amount of fat you eat can make a difference to how well some drugs are absorbed.
- **Checking for interactions with any other medication or drugs.**
This includes medicines that have been prescribed to you, or bought at a

chemist, supermarket or health store, including complementary or alternative therapies. Also be aware that some recreational and illegal drugs can have potentially dangerous interactions with anti-HIV medication.

3

Why is taking your medication properly so important?

- Adherence is the most important element under your control in the success of your anti-HIV treatment.
- Low levels of adherence to HIV treatment regimens lead to the drugs not working effectively and are associated with increases in viral load, a fall in CD4 count, increased risk of disease progression, more time in hospital and an increased risk of death.
- Adherence is particularly important in HIV infection because you can quickly become resistant to anti-HIV drugs if you do not take them at the right times and because cross-resistance (becoming resistant to similar drugs)

limits your future treatment options. Missing doses, taking your doses late or early, taking the wrong doses, or taking a drug in such a way that you absorb too little of it may lead to the development of resistance to your drugs. This is because HIV can develop resistance to a drug if the blood level of the drug is too low to stop the virus from reproducing. As HIV continues to replicate, strains of virus which are able to continue to reproduce despite the drug's presence (drug resistant strains) gain a competitive advantage over the strains of HIV that your medication is still effective against, and form the basis

of the HIV in your body. The booklet in this series, *Resistance* contains more information.

This can have potentially serious results, such as:

- You develop viral resistance, which means that your treatments are likely to stop working and your chance of becoming ill because of HIV is increased, as the amount of HIV in your blood increases and your CD4 count falls.
- You may need to change your HIV treatments, which might include more drugs, be more difficult to take, and have more or new side-effects.

You may become resistant to drugs similar to those you are currently taking. For example, people who become resistant to one of the two currently available non-nucleoside reverse transcriptase inhibitors (NNRTIs) - efavirenz (*Sustiva*) and nevirapine (*Viramune*) usually become resistant to the other drug as well. This is called 'cross-resistance' and the risk varies from drug to drug but it can happen in all the classes of drug used to treat HIV.

Because adherence is so important, some doctors think that in some circumstances it is better for your health to stop treatment completely if you are unable to adhere properly.

It is important that you are aware of the general risks of stopping treatment, and talk to your doctor about whether this is an option for you. Your doctor should talk to you about regular monitoring to reduce the risk that your CD4 count will fall to a level at which you could develop AIDS-defining illnesses.

This is because:

- Your CD4 count is likely to fall back to its pre-treatment level within six months or less, regardless of how high it is now, and will continue to fall after that point.
- If you had an AIDS-defining illness before you started combination therapy, you are five times more likely to experience a CD4 decline back below 200 cells (the at-risk level for further AIDS-related illnesses) than someone who started treatment with a higher CD4 count.
- If you stopped treatment with a CD4 count below 200, you are at risk of developing AIDS-defining illnesses immediately and should discuss with your doctor whether you need to take medication to prevent infections (prophylaxis) before you stop combination therapy.
- If you are taking a drug such as efavirenz (*Sustiva*), 3TC (lamivudine, *Epivir*), or nevirapine (*Viramune*),

which take a long time to clear out of the body, you run the risk of developing resistance during the withdrawal period. If you start treatment again with the same drug, it may no longer work.

Recent evidence suggests that people who take a treatment break may be at greater risk of developing some serious non-HIV related illnesses and have a generally lower quality of life.

7 How many doses of my medication do I need to take?

The best response to anti-HIV treatment is seen when adherence is 100%. Levels of adherence below 95% have been associated with poor suppression of HIV viral load and reduced increase in CD4 count.

- If you are taking once-daily treatments, 95% adherence means missing no more than one dose a month.
- If you are taking your treatment twice a day, 95% adherence means missing no more than three doses a month.
- If you are taking your treatments three times a day, 95% adherence means missing no more than four doses a month.

However, many people with HIV do not manage to achieve such high levels of adherence. Nevertheless, try and miss as few doses of your medication as possible, since any fall in drug levels will offer an opportunity for HIV strains that are less susceptible to the action of the drugs to develop.

A wide range of factors influence people's adherence to medication, and the relative importance of these differ from person to person. This means that there is no one best solution for everyone. Instead, you will need to spend time with your health care team working out what kind of things help or prevent you adhering. One approach is to divide these issues into broad categories, such as:

- You and your medication.
- Your health care team and the kind of support they offer.
- The medicines you are taking.

Everyone's adherence to medication can go through difficult periods. These are some of the things which might affect your adherence to HIV medication.

Being involved in treatment decisions

The best time to start HIV treatment still is not known - currently it is recommended that everybody who is ill because of HIV, or who has a risk of becoming ill (indicated by a CD4 cell count of 200 or below) should start treatment. Some doctors think that there may be advantages to starting treatment at higher CD4 cell counts, such as 350.

However, whenever you decide to start HIV therapy, if you are motivated to take your treatment and have been involved in reaching a decision about when to start, and what medication to start with, you may be more likely to adhere well. Similarly, if you understand why you need to take medication and the benefits of treatment, and how these outweigh the risk of side-effects, you are also more likely to adhere.

Depression and mental health problems

Mental health problems such as depression are linked with low levels of adherence. If you are living with

depression and do not feel that you are able to start an anti-HIV treatment regimen and adhere to it properly, then it might be best to wait until you feel more able to cope. Similarly, if you think that depression is having an effect on your adherence, it is important to seek help and treatment for the depression. Depression in people with HIV is common and many HIV treatment centres have specialist mental health teams. Treatments for depression work just as well in people with HIV.

For more information see the booklet *HIV and mental health* in this series.

Lack of money and housing problems

Lack of money, poor housing and feeling isolated and alone may affect your ability to adhere. Not having enough money could mean that you are unable to eat the foods that your prescription requires. Many HIV organisations can provide advice about money and benefits, and your HIV clinic may have a specialist HIV social worker who may also be able to help or refer you to somebody who is able to help.

Support from other people such as friends or family may also help you to take your medication. On the other hand,

some people may be worried about other people knowing that they have HIV and may not wish to be seen taking their medication. Family responsibilities may also affect your ability to adhere, as you may feel under pressure to put the health care needs of others before your own (see the section on special issues for pregnant women and for children on page 23).

Being homeless or in poor housing has also been shown to lead to lower levels of adherence, as has drug and alcohol use. However, you should not assume that just because you have issues in your life other than HIV, you will not be able

to take your medication properly. There is good evidence that receiving adherence support from your clinic and other HIV support organisations can help you to improve your adherence, even if you are living in the most difficult of circumstances.

What you think about your HIV treatment

People who understand why taking anti-HIV treatment could benefit their health are more likely to achieve high levels of adherence.

If you are thinking about stopping medication because you do not think

that it is working or you are concerned about side-effects, you should make sure that your thoughts and concerns are realistic. NAM's other booklets in this series *Anti-HIV drugs*, *HIV therapy* and *Lipodystrophy*, or introductory Factsheets, could provide a useful starting point. You should also make sure that you discuss any concerns you have about your medication or health with your doctor and you should not stop or alter your medication schedule without first seeking medical advice.

Support for everyone

Your HIV clinic should be an important source of adherence support. Neither your doctor nor any other HIV service provider should assume that you are going to adhere poorly simply because of who you are. As mentioned earlier, many people with HIV have problems with adhering at some time, and people who have good adherence at one time may have poorer adherence at another. You should not have HIV treatments withheld simply on the basis of an assumption about how your personal circumstances might impact on your ability to adhere. Adherence support should be made available to all patients,

as anybody is capable of both high and low levels of adherence.

You should feel able to tell your doctor if you are having problems with adherence. As mentioned before, adherence to anti-HIV treatment can be difficult and your doctor should be prepared to discuss any problems you are having and to work with you to find a solution. The sooner you seek help if you are having adherence problems the better, and if you feel unable to discuss your concerns with your doctor, then try speaking to a nurse or other member of your health care team. HIV advocacy organisations like the UKC (UK Coalition of people with HIV and AIDS,

telephone number 020 7564 2180, www.ukcoalition.org) may also be able to help.

Ask your doctor or other member of your health care team if your clinic has an adherence support policy which outlines the support available to you. Recommended guidelines on the kind of adherence support UK HIV clinics should offer can be read on the website of the professional organisation of the UK's HIV doctors, www.bhiva.org.

Support when starting or changing therapy

If you understand why you are taking anti-HIV therapy and why adherence is

important to prevent treatment failure and the emergence of resistance, then you are more likely to have high levels of adherence. When you first begin taking anti-HIV treatment, being given written information about your treatments to take home and read later helps you to remember what your doctor told you about how and when to take your combination. HIV support organisations may also be able to provide you with information on your medication and how to take it.

Some side-effects are a particular problem when starting new treatment but go away, for most people, after a short

period. These side-effects may include stomach upsets, feeling sick or being sick, bad dreams, or feeling 'spaced out'. It can help to know in advance if your treatment is likely to cause side-effects which interfere with your daily life, looking after children, or work and to make plans to help you cope.

When you start or change therapy you should understand:

- Why you have been given this medication.
 - How often you have to take it.
 - How much you should take.
 - If there are any dietary restrictions.
- If there are any side-effects which might occur and how you might be able to manage them (and when you need to seek advice urgently).
 - Where you can get help and advice (during normal clinic hours and in the evenings and at weekends).

Because taking anti-HIV treatment is a life-long commitment, you may find that you need adherence support on an ongoing basis or at frequent intervals. You should feel able to discuss adherence with your health care team at any time.

Other health care professionals

Many HIV clinics now have nurse specialists and pharmacists who coordinate special adherence support services.

- Mental health specialists such as psychiatrists, psychologists, mental health nurses and counsellors can provide treatment and support if you feel that the state of your mental health means that you have problems adhering.
- Some clinics have nurse specialists who can spend time to discuss adherence with you. This might include
 - how to manage side-effects, or fitting medication in with your lifestyle.
- Pharmacists can sometimes discuss how you should be taking your medication and possible interactions with other drugs and treatments.
- Dietitians can help you make sure that you are eating the right amount of food so that your medication is properly absorbed. They can also give you advice about how to minimise side-effects such as nausea and diarrhoea.
- Social workers can help you with practical issues including housing and money.

Treatments and your lifestyle

You are most likely to take your HIV therapy when it fits in with your existing lifestyle, and decisions about your treatments should be made on an individual basis, taking account of your circumstances. This should include a history of your past treatment experiences, but also your needs and preferences about how often you take your medication, the chances of getting side-effects, and the potential for harmful interactions with other medications.

Looking at your lifestyle needs before you start treatment may mean that you are less likely to encounter adherence problems later on.

Late doses

Taking your medication late can be as bad as missing doses completely, allowing HIV to become resistant to some or all of the drugs you are taking.

The safest approach is to aim to take all your doses at the right time and in the right way, but most people will probably take their medicines late at some time. If this happens very occasionally it will probably make no difference to the success of your medication, however if you regularly take your medication very late, then it could allow HIV to become resistant to your medication.

Some anti-HIV drugs, particularly the protease inhibitors nelfinavir (*Viracept*)

and indinavir (*Crixivan*), are processed more quickly by the body than others, meaning that it is very important to take them at the correct time as the amount of drug in your body will not be sufficient to suppress HIV. This is called a drug's 'half life'.

For some other drugs particularly those in the nucleoside analogue, or NRTI class of anti-HIV drugs as well as the non-nucleoside analogues efavirenz (*Sustiva*) and nevirapine (*Viramune*), the nucleotide analogue tenofovir (*Viread*), and the ritonavir 'boosted' protease inhibitors atazanavir (*Reyataz*), darunavir (*Prezista*), fosamprenavir

(*Telzir*), lopinavir/ritonavir (*Kaletra*), saquinavir (*Invirase*) and tipranavir (*Aptivus*) it may be possible to take your drugs an hour or two late (or early) and for it to have minimal risk for the success of your medication.

Do not assume that because somebody else is able to take their medication late, even if they are taking the same drugs as you, that you will be able to do the same, as the speed and effectiveness with which people process medicines can vary considerably.

If the way you lead your life means that you find it difficult to stick to very strict dosing schedules then talk to your

doctor about the possibility of switching to a combination that requires less rigorous timing.

Going out, travelling, or doing anything which interrupts your normal routine may cause you to have difficulty taking your medication at the correct time. If you know that your normal dosing routine may be interrupted, then try to make a plan that ensures that you take your medication as close as possible to the correct time. For example, taking your pills with you, having a bottle of water to hand, and if you need to take your medicine with food, having a bar of chocolate or some other easy to carry and eat food, may mean that you are

able to take your medicines without disrupting either what you are doing or your medication routine.

Asking people to remind you to take your medication, if you are socialising and the people you are with know you have to take doses of drugs, may also prove useful. Also, keeping spare doses of medicine in places where you may be when you have to take your medicines, such as work, at friends' or relatives' homes, or in your bag may also prove useful. Remember though, always store medicines out of the reach of children.

Dosing frequency

Many HIV combinations now only require once-daily dosing - indeed HIV treatment consisting of just one pill (*Atripla* - FTC, tenofovir, efavirenz), once-a-day is expected to become available soon. There are now very few people who need to take their treatment more than twice-daily.

Dosing requirements may also affect your ability to adhere, particularly if you need to take medication with or without food. You may wish to consider this if you have a preference.

If you forget to take a dose of pills, then take them as soon as you remember and

carry on with your normal dosing schedule. However, you should not take a double dose to make up for a missed dose if you forget a dose completely. Consider talking to your doctor about how flexible the dosing schedule for your regimen is.

Number of pills

This is often referred to as 'pill burden'. Some people find taking a large number of pills difficult to manage. If you have a choice, it's probably best to opt for the simplest combination available to you.

However, many people still experience very real problems with adherence even

when they are taking anti-HIV treatment regimens which are meant to be simple and include fewer doses or pills. Even supposedly easy-to-take HIV treatment regimens have to fit in with the day-to-day realities of living with HIV and taking medication. If you are having problems taking any anti-HIV combination, then tell your doctor or other member of your health care team.

Adherence to T-20

T-20 (enfuvirtide, *Fuzeon*) is an anti-HIV drug from a class known as fusion inhibitors. It is the only anti-HIV drug that needs to be injected. This is

one of the reasons why its use is reserved for people who have quite limited treatment options.

A lot of information and support is provided to people who are prescribed T-20.

Although it is injected as a liquid under the skin twice-daily, it has to be prepared from a powder. Doses can be prepared for injection up to 24 hours before use, so two doses can be prepared together.

T-20 can be injected into the arm, thigh, or abdomen. A different site of injection should be used each day to reduce the chance of the skin becoming irritated

and what are called 'injection site reactions' developing.

A new, needle-free method of administering T-20 is becoming available. It uses high pressure to force the drug under the skin.

Interactions and side-effects

Side-effects are one of the most common reasons for people missing doses. Certain side-effects and interactions are more likely to occur with some regimens and particular drugs. Side-effects can also have practical problems, as they might cause you to vomit or feel sick and so miss

doses, or they might make you tired so you sleep through the time when you should take your dose.

Some anti-HIV drugs can also interact with medicines prescribed to treat other conditions or with recreational drugs. It is important to tell your doctor what other drugs or supplements you are taking. Most HIV specialists are comfortable discussing recreational drug use and at helping people to find treatments which are safer to use with them.

Pregnant women

Low levels of adherence have been noted in pregnant women. It's been suggested that this could be because of concerns about the effect of medication on the baby. If you are pregnant and concerned about the effect your treatments could have on your baby, then speak to your doctor. HIV treatments are very effective at preventing transmission of HIV from mother-to-baby, but only if they are taken correctly.

Some women find that when their baby is born, their routine and priorities change. You should be prepared for this, to make sure that as well as looking after your

baby, you also look after your own health, including taking your HIV medication.

Children

There can be special issues distinct to adherence for children. Children are not all the same, and there are obviously age-related differences which affect adherence. For example, food and fasting restrictions can be difficult for infants and young children. For children of school age, adherence to regimens that require them to take doses at school can be difficult as it could lead to their HIV status being disclosed.

Pill-taking and unpleasant tasting liquid formulations of medications can have a negative impact on adherence for people of all ages, but may be more notable in children.

For more information about adherence in children see the booklet in this series, *HIV and children*.

Simple forgetfulness is a common reason for missing doses of anti-HIV drugs. If you do forget to take your medication don't be too hard on yourself, but do try to learn from the experience what it was that caused you to forget. If you are missing doses regularly, then discuss this with your doctor. It may be possible to make your schedule easier, or change to a more suitable combination. Where this is not an option, talking through your concerns with your health care team may provide you with the support you need to manage your treatment better.

Practice beforehand

Some people have found that taking practice doses of their potential anti-HIV combination helps them to adhere to their actual regimen. This might involve taking sweets or multivitamins for a few weeks in the same quantities and at the same time as you will have to do with your anti-HIV drugs regimen, taking account of any dietary restrictions.

Keeping a diary

Confusion over which pills to take when, and what times to eat or avoid food, may be a problem when starting a new combination. To avoid this, your doctor

or pharmacist can provide a written daily schedule with your prescription, which you can tick off after taking your dose. Some pharmacists offer stickers for medication containers, which have the same function.

Storing and transporting pills

Partitioned containers that you fill once a week or every few days with the individual daily doses are available. With some versions you can take out a single day's dose, or several if you may be away for some time. Your HIV pharmacist should be able to provide one of these boxes free. Make sure that the box you're getting is big enough and that you have

checked with your pharmacist that all your drugs are suitable for storing out of their original container. Some pills deteriorate if not kept correctly. The bottle that indinavir comes in, for instance, contains small canisters that keep the capsules dry and stop them from leaking. You could also use a film container, but the same advice applies.

Some people keep doses in the different places that they could be at the time of pill-taking, e.g. friend's house, handbag, car. Make sure you store medication safely out of the way of children, and remember that extremes of temperature can damage most medications.

Holidays, travel, time off, going out

Think about how going away for a break or on holiday could impact on your adherence. This could include the influence of travel on the times you take your medication, particularly if you are travelling a long way involving a changed time zone. You should try and ensure that you take your medication at the same intervals. Make sure that you take enough medication with you, as securing more supplies might be impossible. You should also travel with your medication in your hand luggage as this is less likely to get lost and means

that your medication is close at hand should you need to take any during your journey. If you are flying or travelling across borders consider obtaining a letter from your doctor giving the name and doses of the medications you are taking and explaining that you need to have the medication with you at all times. This will help ensure that you are allowed to carry the medication in your hand luggage (in case the airline is imposing restrictions on what can be carried) and it may help you with customs officials should you be stopped. This letter doesn't have to mention HIV.

Some countries, most notably the United States, impose entry restrictions on

people with HIV. There is some evidence that a small number of people travelling to the US take a break from their HIV treatment because they are worried about their medicine being found in their luggage at customs and their entry to the US denied. Talk to your doctor before taking any break from your HIV treatment.

Breaking your routine may also have an impact on adherence as you may be away from prompts that helped you remember to take your medication. Think about what these might be and how to overcome them.

Taking your medication away from home may mean that there is an increased

chance that you will have to take it with people who do not know about your health, or who you do not want to know about it. Plan in advance how you might manage this. Simple things such as having a bottle of water by your bed might give you the privacy you need to take your medication.

If you are going out clubbing and think that there is a chance that you may not go home before your next medication dose or doses, then take enough medication to last you. Be aware that door staff may not be able to recognise prescription medication and some people have been asked what their anti-HIV

drugs are or have had them taken off them when trying to get into some clubs. Also if you are going out and are planning to drink alcohol or take drugs which might affect your memory, then try to plan in advance how you might overcome this. This might involve setting an alarm on your watch or telling a friend to remind you when it is time to take your medication. If you are concerned about possible interactions between your anti-HIV medication and recreational drugs then speak to your doctor or another member of your health care team. They should be able to offer advice on safely minimising interactions. Do not skip doses.

Treatment breaks

Taking a break from your treatments might seem attractive, particularly if you are having problems with keeping up with the high levels of adherence required, or if you are having severe side-effects. If you are having problems taking anti-HIV drugs, or with side-effects, discuss these with your doctor or another member of clinic staff rather than stopping treatment alone. They may be able to help solve these problems without needing to stop treatment. You should not take a complete break from your treatment without discussing this with your doctor first as there can be risks involved,

including the emergence of drug-resistance HIV or a worsening of your health.

Sometimes, when people change treatment they are recommended to take a break before starting their new combination of drugs. They will be very closely monitored during this break. Also, if you have certain infections like hepatitis it might be necessary to stop your HIV treatment because of possible interactions and side-effects. Your doctor should tell you if this is the case.

Overcoming difficulties

For some people, taking the pills can be a problem depending on their size, shape

and texture. Always mention problems to your HIV pharmacist. There may be another preparation of the medication available, e.g. a liquid or powder that you might find easier to take than a pill.

Taking an accurate amount of liquid formulations can be a bit tricky. An oral syringe from your pharmacist will help with this process, but you do need to wash and dry them thoroughly between uses. To take a single dose with you when leaving home, ask your pharmacist for an oral syringe cap. Though this will allow you to fill the syringe before you leave, you will need something suitable to protect the plunger. Some people inject

liquid formulations into gelatin capsules, which can be bought from health food stores. This can be a very messy process and ensuring that you take an accurate dose may be difficult, so discuss this with your pharmacist first.

Using a pill crusher can make some pills easier to take. These are available from your HIV pharmacist who will advise you if it is suitable for the drugs you are taking. Pill crushers look like small jars - put the pills inside and then screw on the top. This crushes the pills inside the container.

If you are having ongoing difficulties taking your medication, or are worried, ask for help immediately. Your treatment centre is there to help.

- Adherence means taking your pills in the prescribed doses at the right time, in the right amount and in the right way.
- Missing doses or not taking doses correctly can lead to HIV becoming resistant. This will cause your treatment to fail and limit the drugs you can take in the future.
- Taking your drugs too late or too early can be as bad as not taking them at all.
- A high level of adherence is needed for your HIV treatment to work effectively and you should aim to take every dose.
- Adherence is a process, and involves you, your doctors and other health care providers.
- Adherence support is available and should be offered to everyone taking HIV treatment as part of their ongoing care.
- You might find your adherence easier to manage if your treatments fit in with your lifestyle.
- Pregnant women and children may have special adherence issues.
- Keeping a diary, or using medication alerts might help you to adhere.

adherence The act of taking a treatment exactly as prescribed.

antibiotics Drugs which affect bacteria.

antiretroviral A substance that acts against retroviruses such as HIV.

antiviral A drug that acts against viruses.

CD4 A molecule on the surface of some cells onto which HIV can bind. The CD4 cell count roughly reflects the state of the immune system.

chronic A long-term condition.

cross resistance The mechanism by which HIV that has developed resistance

to one drug may also be resistant to other, similar drugs.

disease progression The worsening of a disease.

dose Measured amount of a drug to be taken at one time.

genotype The genetic make-up of an organism.

lipodystrophy A disruption in the way the body produces, uses and distributes fat.

NNRTI Non nucleoside reverse transcriptase inhibitor, the family of antiretrovirals which includes efavirenz, nevirapine and delavirdine.

protease inhibitor Family of antiretrovirals which target the protease enzyme. Includes fosamprenavir, atazanavir, indinavir, lopinavir, ritonavir, saquinavir, nelfinavir, tipranavir and darunavir.

regimen A drug treatment combination and the way it is taken.

resistance A drug resistant HIV strain is one which is less susceptible to the effects of one or more anti-HIV drugs because of its genotype.

viral load Measurement of the amount of virus in a sample. HIV viral load indicates the extent to which HIV is reproducing in the body.



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