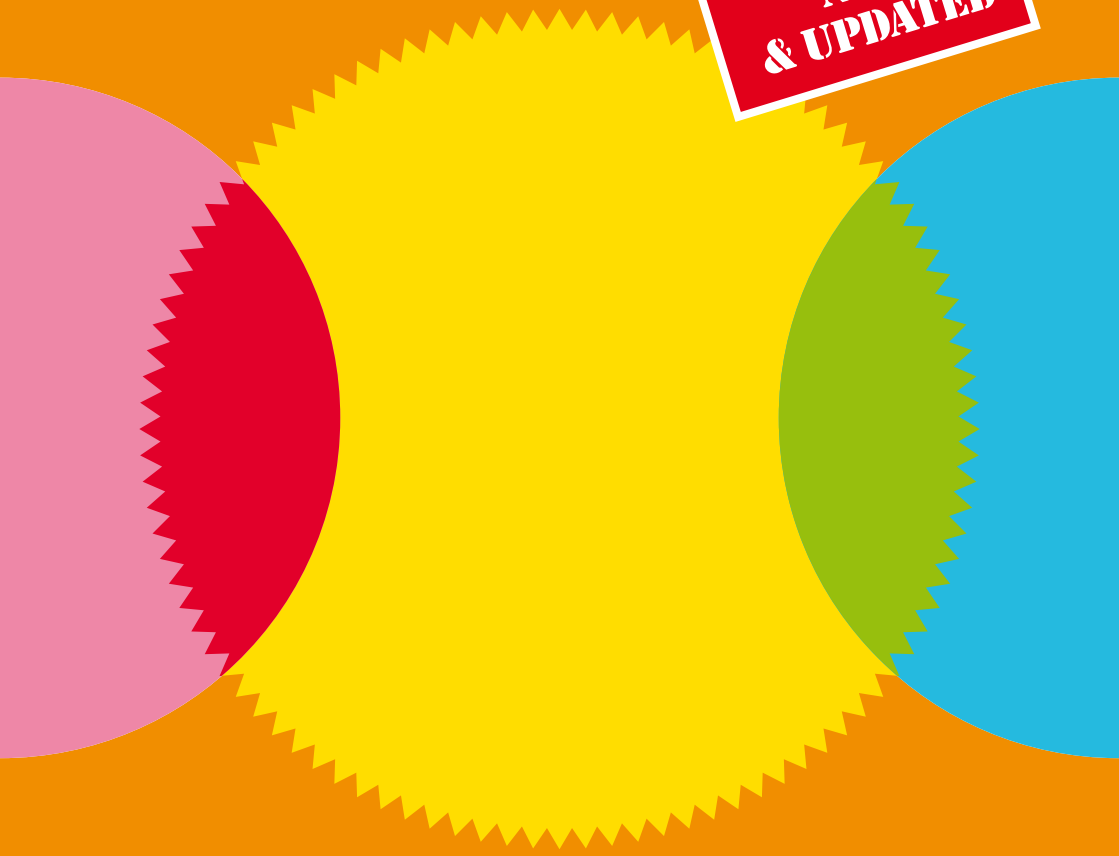
HIV and your quality of life:
a guide to side effects and other complications

July 2012



HIV i-Base
ISSN 2046-7311
www.i-Base.info
Watch out for out-of-date information

Contents

Disclaimer: Information in this booklet is not intended to replace information from your doctor. Treatment decisions should always be taken in consultation with your doctor.

Welcome the i-Base guide to HIV and your quality of life...

This booklet will help you:

- Have accurate, up-to-date information about side effects and what to do about them.
- Get the most out of your relationship with your doctor and other health professionals.
- Feel more in control of your treatment.
- Get better medical care and improved health, and
- Achieve a better **quality-of-life**.

“Everyone worries about side effects before they start treatment.

I have changed treatment four times since 1996. This has been because of side effects or because new research has shown I can change the dose.

Everytime, my quality of life improved more than I expected, even switching from twice-daily to once-daily.

It always takes me a while to decide to change, even when I know that other drugs could be better.

As the benefits from treatment will keep me alive for many years, I want to make sure that my combination is effective, easy to take and tolerable–and that it also gives me the best quality-of-life.”

Section 1:

General information

Introduction

HIV treatment is now more effective and simpler to take than ever before. It involves far fewer side effects and usually fewer pills.

This is the sixth edition of this guide and we have focussed on the meds that are now most widely used.

With over 26 drugs approved and others in development, you can now aim for the best quality of life. It is not just about your CD4 count and viral load.

Negotiating healthcare

This guide has been written by people who are HIV positive. We have taken many of these treatments and experienced many of the side effects

We also understand some of the practical frustrations of being a patient.

Although you may have difficulty with one treatment, there is nearly always something you can do about it. This includes using another drug to treat the side effect, changing to another HIV drug, or, sometimes, altering the dose.

However, many people do not receive as much help in managing side effects as they need.

This may be because communication with your doctor is not as good as it could be.

- Perhaps there was not enough time.
- Perhaps your doctor didn't understand exactly how you are affected.
- Perhaps you just forget to mention a problem.
- Perhaps you did not think or feel it was important.

Sometimes, if side effects continue for several months, you may think it is easier not to mention them at all or to just put up with them.

This is not a good approach.

- Something you think is a side effect may be a symptom of a more serious illness.
- Newer treatments may also have become available since you first reported them.
- You deserve the best quality of life.

Many other people can also help including nurses and pharmacists.

Outline of this guide

The first section of this booklet includes general information, including how to talk with your doctor and your rights as a patient.

The second and third sections include information on each side effect or set of symptoms or important health topics.

The fourth section focuses on issues that may or may not be directly related to HIV and side effects, but which are related to ageing. This section also includes links and references.

This guide is also online with additional text. Earlier editions have been translated into other languages. Many of these are available on the i-Base website:

www.i-Base.info

Changes to this edition

This edition includes the following changes:

- It has been updated to include side effects of recently approved drugs.
- Information on side effects of drugs that are now rarely used has been reduced in the print edition. This information is still available online.
- We have expanded information about long-term health even if this is not a side effect. This includes the sections on your heart and bone health.
- We have expanded the sections on HIV and ageing because this an essential part of living well with HIV.
- We have included new sections on diet and exercise. These are important additions. They explain how to choose a balanced diet and how to be more active - and the impact this can have on your health.
- The references available online have been updated. This includes more than 380 research studies or clinical guidelines. These are listed by subject with hyperlinks to the online publications.

  These include:

- The product information for each drug.
- Treatment guidelines (from the UK, Europe and the US).
- Studies that focus on safety of HIV drugs.

Whenever possible we selected references that provide free full text access online.

If you have a question about anything you read here, you can call the i-Base phoneline or email a question to the online Q&A service.

Feedback and comments

We welcome feedback and comments. Please see page 105 or use the online survey:

www.surveymonkey.com/s/7CCWBW2

General questions

What are side effects?

A drug is usually approved to treat a specific illness. Anything else it does is called a side effect.

Sometimes side effects can be helpful, but more often they are a problem.

Side effects can be annoying, difficult and in rare cases, extremely serious.

In this booklet we mainly focus on side effects of HIV antiretroviral drugs (ARVs).

Side effects are also called adverse events or referred to as drug toxicity.

Do all drugs have side effects?

Every drug is likely to have some side effects for some people. In most cases these will be mild and easy to manage.

Sometimes they are so mild that they are not noticed. They usually only affect a small proportion of people.

Serious side effects, although possible, only occur rarely.

How common are side effects with HIV drugs?

Most HIV drugs have a low risk of serious side effects.

However, the information about potential side effects can sound worrying. Even common, over-the-counter, medicines like aspirin or paracetamol have many potential side effects (see Table 1).

Most people starting HIV treatment report one or more side effects. Sometimes this is because when we start a treatment we are more sensitive to anything that happens, even though it may not be a side effect.

People in studies taking a placebo often report high rates of side effects.

Not everyone taking drugs will have the same effects. What is important is how they affect you and what you can do about them.

Symptoms vs side effects

The word symptom is usually used for any change in how you feel that you could report to your doctor. For example, feeling tired, or having diarrhoea are both symptoms that could be side effects.

Other side effects can only be seen after a lab test, for example, high cholesterol or raised liver enzymes.

The symptoms of many common side effects are similar to symptoms of illnesses. Your doctor needs to know about every symptom in order to be able to decide whether it is caused by treatment (a side effect) or a different illness.

Different treatments are needed when a symptom relates to an illness.

Why do side effects occur?

Developing drugs is difficult and complicated. Drugs are designed to work against a specific illness. In doing this they often interfere with other body systems.

It is difficult to make a drug that targets one part of the body without affecting others.

Every new drug is developed to hopefully be better than existing drugs.

The current drugs may not be perfect, but they are better than they have ever been. And drugs in development now will hopefully be better still.

Table 1: Side effects listed for aspirin

Dyspepsia (digestive problems), nausea, vomiting. Less commonly, irritation of the gastrointestinal mucosa may lead to erosion, ulceration, gastrointestinal bleeding. Hepatotoxicity (liver toxicity), which occurs rarely.

Hypersensitivity reactions including urticaria (rash), rhinitis (nasal problems), angioedema and severe bronchospasm (blocked airways).

May cause salt and water retention as well as a deterioration in kidney function.

Source: http://www.medicines.org.uk

Where can I get more information?

A leaflet should be included with every medicine that you are prescribed, including HIV drugs. If your hospital doesn't provide this then ask for it.

This leaflet is important. Even when the information is simplified, it should include:

- How and when to take the drug.
- Whether you need to take it with food.
- Common and serious side effects.
- Interactions with other drugs.

Sometimes the leaflet is much more detailed, usually in small print and is similar to the Summary of Product Characteristics (SPC).

The SPC is a detailed document produced for every new drug. It is available free on the European Medicines Agency (EMA) website.

http://www.ema.europa.eu

The information in the SPC includes more detail about:

- All reported side effects and their frequency in studies.
- The studies that led to approval, and
- Food and drug interactions, and doses, including dose changes.

Information on each HIV drug on the i-Base website includes a direct link to the EMA web page for that drug.

http://i-base.info/guides/category/arvs

How are side effects reported?

The risk of side effects should always be given in real (numerical) terms. A 10% risk means you have a 1 in 10 chance that it will occur. This is the same as saying if 10 people use the drug, one person is likely to get the side effect.

Sometimes the risk is also described with more general words, like rare, or common.

Language is very important but it is not always used correctly.

A side effect that occurs in more than one in 10 people is 'very common'. A rare side effect has to occur in less than one in 1,000 people, see Table 2.

When a drug is first studied, every side effect is recorded, even if it cannot be directly linked to the drug being studied.

This is one reason why the leaflet that comes with any drug usually has a such a long list of potential side effects.

The risk of getting most of these listed side effects is usually very low - often less than 1 in 100 or 1 in 1000.

Table 2. Definitions for frequency

Very common	affects 1–10 people in 10. ie 10% chance or higher
Common	affects 1–10 people in 100. ie 1% to 10% chance
Uncommon	affects 1–10 people in 1,000. ie 0.1% to 1% chance
Rare	affects 1–10 people in 10,000. ie 0.01% to 0.1% chance
Very rare	affects less than 1 in 10,000. ie less than a 0.001% chance.
Not known	frequency cannot be estimated from the available data.

If side effects only become apparent after the drug has been approved, as with lipodystrophy, the drug leaflet may not have this latest information.

Some side effects are only discovered after a drug has been approved. However, most drugs become safer over time, as more people use them, and more information is collected.

If you are feeling more anxious or nervous, are not sleeping properly, have a lower sex drive or have lost your appetite, it is important that your doctor understands this.

Starting treatment for the first time?

Everyone worries about the risk of side effects before they start treatment.

Before choosing your combination, ask for information about each of the drugs you might take. Ask about the likelihood of side effects. Ask what percentage of people had side effects related to each drug and how serious they were.

Before starting treatment, ask for the out-of-hours phone and email contact details for your clinic.

You may be asked to join a study looking at side effects. These studies are important to define the extent of side effects when different drugs are used together.

People in studies are monitored more carefully and more frequently, so you may get better care.

Research is essential if we want new and better drugs in the future.

Can I change drugs easily?

You should be offered at least two options whenever you start or change treatment. Ask about the advantages and disadvantages for each one.

Some people are not told that they have a choice. This is not right. Even if your doctor prefers one combination, you need to be involved in this choice.

If you have problems with the first combination, you can easily modify the drugs.

There are more than 26 HIV meds in the UK, including several that include more than one drug in each pill. While you can't quite mix and match them, if one or more of the drugs in your combination is difficult to tolerate, you can change it for another.

If you change a drug because of tolerability, you can usually use it again later if you need to *[except for abacavir - see page 48]*.

Just because you used a drug once, does not mean you have 'used up your option' of using it again in the future.

Usually side effects improve after the first few days, weeks or months, but sometimes they don't. See the sections on each side effect in this booklet for an idea of how long you should put up with them before changing.

You do not have to continue with a drug to prove anything to yourself or your doctor. If something is wrong, ask your doctor to change to something else. Some drugs are just not for everyone.

Can I know if I will get side effects?

You cannot know whether you will get side effects from a drug until you take it.

The only way to know is to try, and you will be carefully monitored.

Are side effects different in men and women?

Generally, side effects are similar between men and women. Sometimes, other factors, such as weight, may explain any differences as smaller people may absorb relatively higher drug levels.

Many trials enroll too few women to be able to study differences between men and women. However, more recent studies have not shown differences in the type of side effects experienced.

One exception is that women have higher rates of side effects with nevirapine (both liver toxicity and rash), which is why careful monitoring is essential. This risk is related to CD4 count. Women should not start with nevirapine if their CD4 count is over 250 cells/mm^3. The cut-off for men is 400 cells/mm^3.

There may also be differences relating to lipodystrophy and gender *(see pages 67–75)*.

What about side effects and adherence?

Adherence is the term for taking the meds in your combination exactly as they are prescribed. It includes taking them on time and following any dietary advice.

If side effects affect your adherence your doctor needs to know.

There is a special section about adherence and side effects on page 22.

Getting your doctor to help…

Many of us ***underestimate*** side effects when we talk to our doctor.

- We don't like to make a fuss.
- We say they are more manageable than they really are, or
- Sometimes we forget to mention them at all.

Unfortunately, some doctors think that we ***overestimate*** side effects.

- They think we exaggerate side effects, and that they are not really as bad as we say.

This means there can be a big difference between what is actually going on and what your doctor thinks is going on.

This is one reason that side effects are often under treated.

Tell your doctor about any problem. This should not just be how you feel at the time, but how the side effects change when you are not seeing your doctor.

If you don't say something, nothing will change.

i-Base can answer
your questions
by phone, email or online:
0808 800 6013
questions@i-Base.org.uk
www.i-base.info/questions

What happens if side effects continue?

If the first treatment you are given to help with a side effect does not work, there are usually other drugs that you can use.

In this guide we list a range of options, including alternative treatments, for each main symptom. If one doesn't work then try others.

Changing one HIV drug for another is also an important option.

Stopping treatment is not generally recommended, but for some patients in some circumstances, this may still be considered. This would be when the benefit of treatment is low but when side effects are difficult or severe.

Can I report side effects officially?

In the UK, both patients and healthcare professionals can report side effects directly to the Medicines and Healthcare products Regulatory Agency (MHRA).

This is through the Yellow Card scheme.

This contributes to an important safety database, especially for new and unexpected side effects.

Side effects from new drugs often emerge after approval, and it is worth reporting them even if you aren't sure.

http://yellowcard.mhra.gov.uk

How to talk about side effects to your doctor

If you want your doctor to help, you need to describe your symptoms clearly and to say how they affect your life.

Your doctor can then check for other possible causes. For example, that diarrhoea is not related to food poisoning, or that sexual problems are not related to low testosterone.

The best way to do this is to keep a side effect diary. Record everything and take this when you see your doctor.

An example is included on page 16. Use a new sheet of paper if you need more space and take this to your appointment.

For each symptom, include information about how often, for how long, how badly - and the impact on your life.

How often?

How often do you get symptoms?

- Once or twice a week? Once every day? 5–10 times a day? etc
- Do they occur at night as well as during the day?

How long?

How long do the symptoms last?

- If you feel sick or get headaches, does this last for 20 minutes, 3–4 hours, or different lengths of times?
- Is there a pattern? Is it two hours after each dose? or every morning etc?

How badly?

How bad are the symptoms?

- Rate them on a scale (from 1 for mild to 5 for severe).
- A scale is a useful way to describing anything that involves pain.
- Recording severity when side effects occur is better than trying to remember later.
- Does anything help? If yes, write this down too.

How does it affect your quality of life?

How do the symptoms affect your daily life? This can really help your doctor understand how difficult the side effects are for you.

- Many people put up with chronic diarrhoea without explaining to their doctor that it stops them ever going to the pub or the cinema. Tell your doctor if this is the case.
- If you are feeling more anxious or nervous, are not sleeping properly, or have a lower sex drive, it is important that your doctor understands this.
- If you have taste changes, or are too nauseous to eat properly, it is important for your doctor know.
- Symptoms of lipodystrophy, the term for body fat changes, are difficult to measure. If this worries you it can change your whole outlook on life. Are you less social or less confident? Is this contributing to depression?
- Do side effects make you less strict at taking your meds?

Side effects diary

Use this page to record any changes in your health that could be related to side effects. You may not get any side effects but if you do, then this diary will be useful. The most common side effects are listed below but include others even if they are not listed here.

1. Feeling anxious
2. Mood swings
3. Feeling depressed
4. Sleep disturbance
5. Vivid dreams
6. Nightmares
7. Feeling tired
8. Headache
9. Rash
10. Nausea/vomiting
11. Yellow eyes or skin
12. Diarrhoea
13. Stomach pains
14. Taste or appetite
15. Weight gain
16. Weight loss
17. Body shape changes
18. Sexual changes
19. Hair loss
20. Tingling in hands/feet
21. Pain in hands/feet
22. Dry skin
23. Eyesight changes
24. Other(s) specify

Side effect	**Date**	**Time(s)**	**Scale:** 1= mild to 5 = severe
			1 2 3 4 5
			1 2 3 4 5
			1 2 3 4 5
			1 2 3 4 5
			1 2 3 4 5
			1 2 3 4 5
			1 2 3 4 5
			1 2 3 4 5
			1 2 3 4 5

Other comments and questions to ask your doctor:

How side effects are graded in research studies

Most information about the risk of side effects comes from clinical studies and research.

This is why it is important to report all side effects if you take part in a study.

Trials collect information about:

- All potential side effects.
- How often side effects occur, and
- How serious they are.

But studies use small numbers of people for relatively short periods. So sometimes rare side effects are only discovered after a drug is approved and has been widely used for many years.

In studies, each side effect graded from 1 to 4. Grade 1 is mild and grade 4 is serious, life threatening or requiring hospitalisation.

GRADE 1 (Mild)

Transient (goes away after a short time) or mild discomfort; no limitation in your daily activity; no medical intervention/ therapy required.

GRADE 2 (Moderate)

Your daily activity is affected in a mild to moderate way – some assistance may be needed; no or minimal medical intervention/therapy required.

GRADE 3 (Severe)

Your daily activity is markedly reduced – some assistance usually required; medical intervention/therapy required, hospitalisation or hospice care possible.

GRADE 4 (Potentially life threatening)

Extreme limitation to daily activity, significant assistance required; significant medical intervention/therapy, hospitalisation or hospice care very likely.

Grading for some common side effects (from the United States Division of AIDS) is shown in Table 3.

Table 3: Examples of how common side effects are graded by level of symptoms

Side effect	Grade 1	Grade 2	Grade 3	Grade 4
Diarrhoea	3–4 loose stools a day OR mild diarrhoea lasting less than one week.	5–7 loose stool a day OR diarrhoea lasting more than one week.	Bloody diarrhoea OR over 7 loose stools a day OR needing IV treatment OR feeling dizzy when standing.	Hospitalisation required (possible also for Grade 3).
Fatigue	Normal activity reduced by less than 25%.	Normal activity reduced by 25–50%.	Normal activity reduced by over 50%; cannot work.	Unable to care for yourself.
Liver toxicity: AST or ALT leve	1.25–2.5 Upper Limit Normal	2.5–5.0 x ULN	5.0–7.5 x ULN	more than 7.5 x ULN
Mood disturbance	Mild anxiety, able to continue daily tasks.	Moderate anxiety/dist-urbance, interfering with ability to work, etc.	Severe mood changes requiring medical treatment Unable to work.	Acute psychosis, suicidal thoughts.
Nausea	Mild OR transient, but reasonable food intake.	Moderate discomfort OR intake decreased for less than 3 days.	Severe discomfort OR minimal food intake for more than 3 days.	Hospitalisation required.
Rash	Redness or itchy skin on part or whole body.	Rash that breaks skin, hard or soft pimples OR light peeling/scaling.	Blistering, open ulcers, wet peeling, serious rash over large areas.	Severe rash, Stevens Johnson syndrome. Severe broken skin.
Vomiting	2–3 episodes a day OR mild vomiting for less than one week.	4–5 episodes a day OR mild vomiting for more than one week.	Severe vomiting of all food and fluids over 24 hours OR needing IV treatment OR feeling dizzy when standing.	Hospitalisation for IV treatment (possibly also for Grade 3).

Side effects, drug levels and genetics

Most drugs are approved at one standard dose even though different people absorb drugs differently. This can be related to differences in our genes and is a new area of research called pharmacogenetics.

For example, tiny differences in your DNA can explain the differences in levels of drugs including efavirenz, nevirapine and atazanavir.

Just as the blood levels of a drug affects how effective it is, they also affect the chance of side effects.

Some HIV drug levels can be checked using a test called therapeutic drug monitoring (TDM). The dose can then be changed if they are too high or too low.

- Protease inhibitors, NNRTIs and integrase inhibitors ***can*** be measured.
- Nukes (AZT, 3TC, FTC, ddI, abacavir and tenofovir) ***can not*** be measured. This is because the important levels of these drugs are inside cells and the tests measure drug levels in blood.

Some clinics use TDM routinely but in others you may need to ask for it.

When should Therapeutic Drug Monitoring (TDM) be used?

TDM is important when routine recommended dosing is not always appropriate, for example:

- In children.
- In people with pre-existing liver or kidney damage.

TDM is important for children and people with pre-existing liver or kidney damage ... and... whenever drug levels or drug interactions may be linked to side effects.

- When drug levels may be linked to side effects. If you get yellow eyes with atazanavir TDM can help find an effective lower dose.
- When drug interactions are a concern. For example, when antacid drugs like omeprazole reduce levels of atazanavir and cause treatment to fail.

TDM involves taking a blood sample, usually after you have been on a treatment for at least two weeks.

The hospital needs to know the exact time that you took your previous dose in order to interpret the results.

Sometimes a sample is taken just before you are due to take your next dose, and sometimes it is also taken 2–3 hours afterwards.

TDM is part of an individualised approach for specific groups of people.

Information on TDM:

http://www.lab21.com

Information on drug interactions:

http://www.HIV-druginteractions.org

http://www.HIVpharmacology.com

Changing HIV drugs

Some symptoms in the first few weeks of treatment may be caused by immune stimulation of your body getting better. So what you think may be side effects may not be related to the drugs at all.

If your initial symptoms are only mild or moderate, seeing whether they settle down before changing treatment, can be good advice. Some side effects become much easier after the first few days and weeks of treatment.

If side effects are more serious or difficult it is important to switch drugs.

Changing to another treatment is usually easy and will not affect your future options.

- Switching drugs can improve your quality of life and still keep your viral load undetectable.

The decision to change treatment in order to manage side effects will depend on:

- The other drugs available.
- Whether the side effects are likely to get worse if don't change.
- Whether the side effects are related to drugs. Even though there may not be a known link, this may be a new report, and you may be the first person to experience this.
- Never just stop or interrupt treatment without contacting your doctor first.
- If your current combination is not your first treatment, you may have fewer options.

Close monitoring after changing a drug will help you know whether that treatment was causing the symptoms.

Switching nukes

Most combinations involve two nukes. the most commonly used nukes are 3TC, FTC, abacavir and tenofovir.

Guidelines recommend that people using older nukes like AZT, d4T or ddI should switch to tenofovir or abacavir as these drugs have fewer side effects.

So long as you haven't developed resistance to other nukes, you can switch one for another. The exceptions are:

- Do not use 3TC and FTC together
- Do not use AZT and d4T together
- Do not use d4T and ddI together
- Do not use ddI and tenofovir together
- There may be a caution against using abacavir and tenofovir together.

Switching between PIs

Switching from one protease inhibitor (PI) to another is also straight-forward, especially if both PIs are being boosted by 100 mg or 200 mg of ritonavir.

However, some people find ritonavir a difficult drug, even at 100 mg/day.

Although not generally recommended, atazanavir and fosamprenavir can also be used without ritonavir.

If you want to do this, your drug levels need to be checked (see page 19).

Switching NNRTIs

Nevirapine and efavirenz have similar potency but some different side effects.

Nevirapine is more linked with skin rash and liver toxicity – usually in the first 1-2 months of treatment.

Efavirenz is linked to mood disturbance, disturbed sleep patterns and vivid dreams (called CNS side effects) when starting and more rarely in the long term.

You should be able to switch from one to the other without stopping treatment or changing your other drugs.

Two newer NNRTIs may also become more widely used as options for people who have difficulty with efavirenz or nevirapine.

Etravirine (Intelence) is a newer NNRTI that can be used if you have difficulty with nevirapine or efavirenz. Etravirine does not cause CNS side effects.

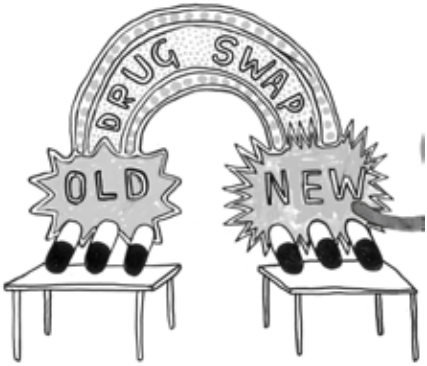
Rilpivirine (Edurant) is another new NNRTI. It still has CNS side effects, only at half the rate compared to efavirenz.

Switching between different classes

It is also easy to switch between different type of HIV drugs.

For example, people who have difficulty taking efavirenz often switch this drug to atazanavir/ritonavir or to darunavir/ritonavir or to raltegravir.

Similarly, people who have trouble with a protease inhibitor can often switch to an NNRTI or an integrase inhibitor.



Using new drugs and new classes of drugs

One of the advantages of new drugs is that they hopefully have fewer side effects.

There are several new drugs available including some that work in different ways.

These include:

- Raltegravir (an integrase inhibitor)
- Maraviroc (a CCR5 inhibitor)
- Other new drugs in development

Each of these drugs has their own side effects, and advantages as a switch options.

For example, raltegravir does not increase cholesterol or triglycerides.

As each new drug becomes more widely used, they will probably be used as switch options.

Each choice will be based on your individual treatment history.

It may also depend on how the drug is licensed, on drug cost, and on which clinic you attend. If it is important to get access to a new drug, it may be worth changing your clinic.

Side effects and adherence

Whether you are starting your first treatment or have been using HIV drugs for a long time, your doctor should have talked to you about the importance of adherence.

This is the term that describes taking the medications exactly as they are prescribed.

This includes:

- Taking them on time.
- Following any dietary advice (ie with or woithout food).
- Taking them everyday: weekdays, at weekends and on holiday.

Not getting adherence right leads to treatment failure and resistance.

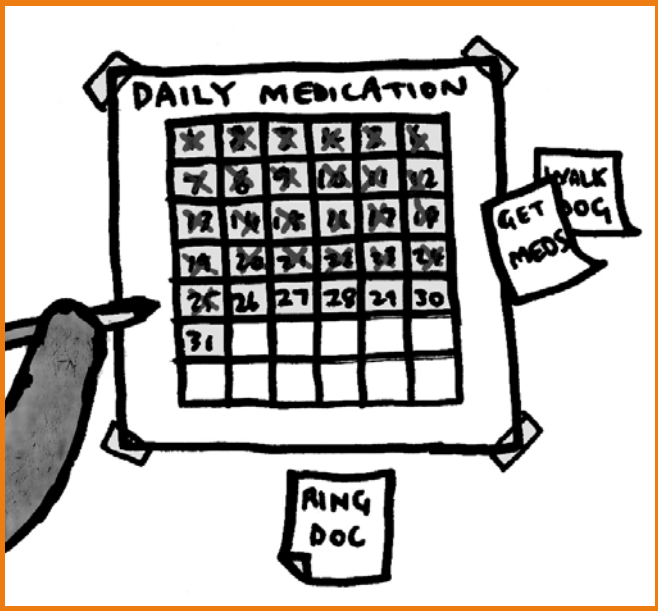
There is a link between adherence and side effects.

...If you are getting side effects, take them seriously and tell your clinic...

If you get side effects, take them seriously and tell your clinic.

Many treatments help with nausea and diarrhoea. You can be given a small supply of these to take to prevent side effects when you first start treatment. You should also be able to collect these easily from your clinic if you get symptoms.

Adherence can be more difficult when medications make you feel less well.


DAILY MEDICATION
WALK DOG
GET MEDS
RING DOC

You and your doctor

A good relationship with your doctor and health workers can help your health in the long-term.

Nurses and pharmacists can give you support and advice on all aspects of your treatment. This includes adherence and side effects.

They can make referrals to other professionals, including dieticians, psychologists and social workers.

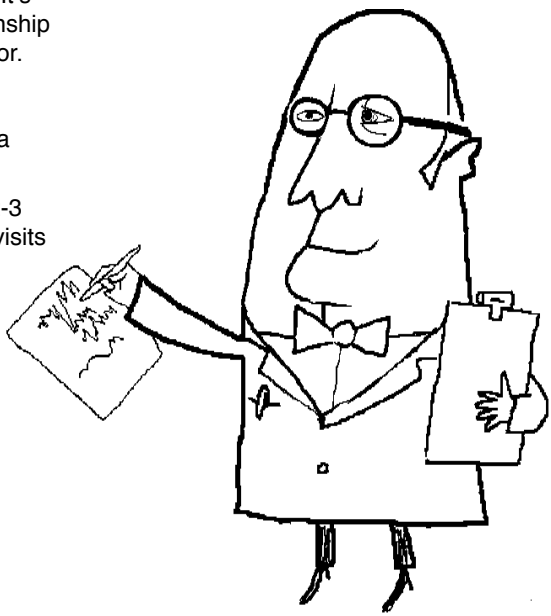
Both you and those involved in your care have certain rights and responsibilities. The following lists include some of your rights and responsibilities as a patient.

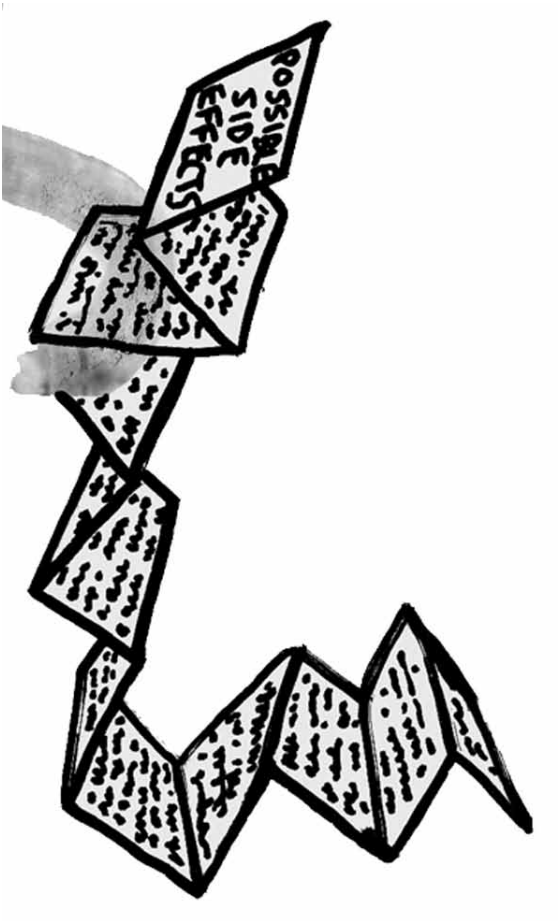
Some of your rights as a patient...

- To be fully involved in all decisions about your treatment and care.
- To be seen within 30 minutes of your appointment. If they are running late, you should expect an explanation.
- To be treated with respect and confidentiality.
- To have different options for treatment explained to you. This should include the risks and benefits of each option.
- To have your doctor or nurse explain any test results.
- For your records to be kept securely. They should be made available for you to see if you ask.
- To choose whether to take part in research trials. This should not affect your current and future care.
- To be able to make a complaint about your treatment. Any complaint must be fully investigated. Again, this must not affect your future care.
- To have a second opinion from a suitably qualified doctor.
- If you write to your hospital or clinic, you should have a written response within 14-28 days.
- To change your doctor or treatment centre without it affecting your future care. You do not have to give a reason for changing doctors or clinics. However, if there has been a problem, then giving a reason can sometimes help resolve the problem.
- To have test results and a summary of your treatment history forwarded to your new doctor or clinic.

Things you can do to help

- Find a clinic that is convenient to you and that you feel comfortable with.
- Find a doctor who you like. If you are a woman and want to see a female doctor then ask for this.
- If you are a gay man and want to see a gay doctor, this may be available and may affect your choice of clinic.
- Turn up for your appointments on time. Tell the clinic if you can't make it. Then they can give your slot to another patient.
- Make a list of things you want to discuss with your doctor. Remember to take it to your appointment!
- Ask to see the same doctor at each visit at least until you are settled with your care. This is important. It's difficult to develop a good relationship if you always see a different doctor. Once you are more settled, the advantages of sometimes seeing a different doctor include getting a second opinion and perspective.
- Have your routine bloods taken 2-3 weeks before your regular clinic visits so the results are ready for your appointment.
- Treat all people involved in your care with the same respect you would wish to receive yourself.
- Listen carefully to the health advice that you are given, and act upon it.
- If you don't understand something, ask your doctor to explain it again or in a different way.
- Be honest with those caring for you. Tell them about any other drugs that you are taking. This includes alcohol, legal and illegal drugs and complementary treatment.
- Be honest about your level of adherence. If the people managing your care don't know you are having problems, they can't help.




POSSIBLE
SIDE
EFFECTS

Section 2:
General symptoms

Diarrhoea

Feeling sick (nausea and vomiting)

Feeling tired (fatigue)

Insomnia (not sleeping well)

Mental health

Sexual health

Diarrhoea

Most HIV medications list diarrhoea as a potential side effect even though it only affects a minority of people. Ritonavir (Norvir) and other protease inhibitors are particularly associated with diarrhoea.

Diarrhoea is a common side effect, but it is often not treated because people find it difficult to discuss.

Diarrhoea can be caused by HIV itself, by complications of HIV, and by HIV drugs.

Diarrhoea includes looser and more watery stool and increased frequency.

It is important that diarrhoea is managed properly by your doctor. Diarrhoea if moderate or severe can lead to dehydration, poor absorption of nutrients and drugs, weight loss and fatigue.

Long term use of early HIV drugs (some nukes) or heavy alcohol use can damage the pancreas. This can upset the production of enzymes from the pancreas that help you digest food, and cause diarrhoea.

Diarrhoea can be related to something you have eaten, other infections and travel to other countries.

Most of us get diarrhoea at some point and having a lower CD4 count increases this risk. Most diarrhoea is self-limiting lasting just for a few days. However, sometimes it can last for a few days, weeks, months or, in some cases, years.

Anything lasting more than a few days is serious enough to talk to your doctor about.

Finding the cause

Often diarrhoea is temporary and may be due to starting or changing treatment. Symptoms often reduce within a few days or weeks as you get used to the meds.

In this case, short courses of anti-diarrhoea medications such as loperamide (Imodium) or diphenoxylate and atropine (Lomotil) can work.

If diarrhoea persists for more than a few days, and is not directly linked to starting a new combination, it is important to run tests to check that it is not being caused by bacterial or parasite infections.

A short course of antibiotics can clear a bacterial infection, and can be prescribed where an infection is suspected but cannot be isolated.

Heavy alcohol use, or the class of HIV drugs called nukes (NRTIs) can also change the way your body responds to diarrhoea. This can be checked by testing a stool sample for faecal elastase (FE1). If pancreatic enzymes are low they can be replaced using supplements.

Non drug-related causes

If diarrhoea continues for more than a few days, ask for a stool sample to be analysed. Some tests can take a couple of weeks for the results.

Depending on the severity and history of the symptoms and following examination, your doctor may prescribe a course of antibiotics along with anti-diarrhoea drugs to reduce the amount of times you need to go to the toilet.

If lab tests fail to show any bugs, and if symptoms persist, then your doctor may want to perform an endoscopy. This will get a biopsy (a tiny piece of tissue) to be sent for analysis in the laboratory. This can rule out other bowel problems such as colitis. As diarrhoea can be a symptom of other illnesses, it is important to run these tests.

Management and treatment

If nothing shows up in these tests, then the treatment of the symptom itself becomes important.

If you are tolerating your combination generally, you may be able to manage diarrhoea with anti-diarrhoeal drugs or dietary changes, both of which are listed below.

Depending on your treatment options you can also look at changing the drug that is likely to be causing this. Some HIV drugs cause diarrhoea more than others.

Diet

- Drink plenty of fluids to replace the water being lost due to diarrhoea.
- Reducing milk and dairy products in your diet will help if you are lactose intolerant. Alternatives such as rice and soya milk do not contain lactose.
- 'Rice water' works as a starch. Boil a small amount of rice in water for 30–45 minutes (or microwave for a shorter time). Flavour with ginger, honey, cinnamon or vanilla when it cools, and then drink during the day.
- Eat less *insoluble* fibre. Foods that contain insoluble fibre include vegetables, whole wheat breads and cereals, skins, fruit, seeds and nuts.
- Eat more *soluble* fibre. This is particularly helpful when watery stools are a problem as they help to absorb the excess water and bulk the stool. Soluble fibre is in white rice, pasta. Ispaghula (psyllium) husk (i.e Fybogel or Isogel) and oat bran tablets increase soluble fibre in your diet.
- Reduce caffeine intake as this can can cause the gut to speed up and result in more bowel movements. Caffeine is in coffee, tea and cola. Recreational drugs can have the same effect.
- Eat less high fat and high sugar foods.
- Eat foods rich in potassium such as bananas, peaches, potatoes, fish and chicken. Potassium is lost when you have diarrhoea.
- Try eating live yoghurt to enhance the helpful bacteria in your gut. If you have a problem with dairy products then acidophilus can be taken in pill form. If your CD4 count is under 50 this may not be advisable.
- Whatever changes you make to your diet, make sure it remains balanced. Don't live on just a few food products, as you will be missing out on essential vitamins and minerals. Ask to see a dietician if you want advice and support about your diet.

Medications and supplements

- Antibiotics are prescribed if a bacterial infection is suspected or detected.
- If pancreatic enzymes are low, supplements like pancrelipase (Creon) or pancreatin (Pancrex) can return them to normal levels.
- Fluid and electrolyte replacement (such as dioralyte and sports rehydration solutions like Gatorade etc) are given to rehydrate the body. Recipes are online to make these yourself: ie 1 teaspoon salt, 8 teaspoons sugar, 1 litre of fluid (water, soup, diluted yogurt - but not sugar-based drinks).
- Imodium (loperamide), Lomotil and codeine phosphate are the drugs most commonly prescribed for diarrhoea. They work by slowing gut motions and the speed that you process food, hopefully reducing the number of stools each day. Take with water 30 minutes before food, or as prescribed.

  Your doctor will normally prescribe these first and, for many people, these medications work well. It is important that the medications are taken regularly until the diarrhoea is well controlled. Start with low doses. If you are taking the maximum dose (8 pills a day for Imodium) and it is still not working, ask your doctor for something else.
- Glutamine has been used experimentally to try and improve bowel function. There is still some debate about the dosage – opinion ranges from 5 to 40 g a day. It is available either as a powder that must be dissolved in water or a regular pill.
- Bulk forming laxatives are useful when watery stools are a problem. They absorb fluid and bulk out the stool – and lengthen the time the stool stays in the bowel. These drugs are generally taken following a meal and you should not drink for 30 minutes after taking them. Don't take at the same time as HIV meds. Brands include Fybogel, Isogel, Regulan, Celevac and Normacol.
- Studies on oat bran tablets taken by people with diarrhoea using protease inhibitors were successful and work on the same principle. The dose was 2–3 oat bran tablets before meals or after each protease inhibitor dose.

Treatments:

- Pancreatic enzymes supplements like Creon or Pancrex (if pancreatic insufficiency has been shown)
- Diet changes
- Dioralyte (electrolyte replacement)
- Imodium (loperamide) or Lomotil
- Ispaghula (psyllium husk or seeds)
- Glutamine
- Codeine, tincture of opium or MST (slow-release morphine sulphate)
- Octreotide injections

Diarrhoea needs to be treated as it can lead to dehydration, poor absorption of nutrients and drugs, weight loss and fatigue.

Palliative care and pain management teams manage chronic diarrhoea, neuropathy and other symptoms that may involve pain or mobility problems.

Fig 1: How opiod anti-diarrhoeals work

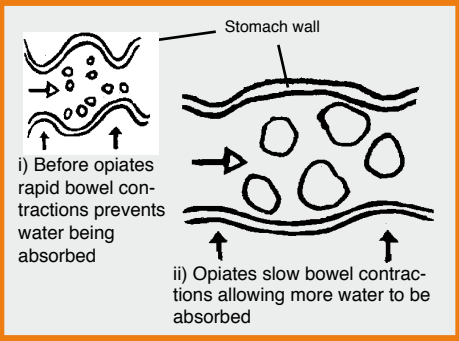
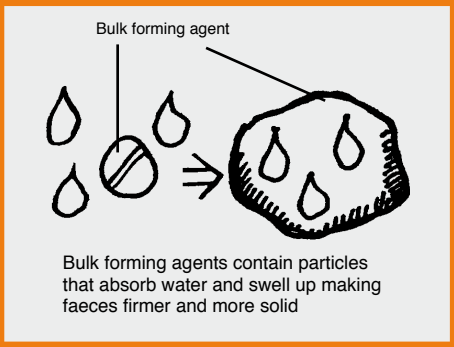


Fig 2: How bulk-forming agents work



-as a last resort...

Slow release morphine sulphate (MST) or octreotide injections can be used if all the usual medications have not worked– although it is used less to control side effects and more to treat other causes of diarrhoea. The slow-release formulation of MST means that low doses of the drug are provided throughout the day. It comes in a wide range of strengths, each coloured differently, so you can be very careful about only taking the dose that you need.

The liquid formulation of morphine sulphate can be used for diarrhoea that occurs at specific times – ie in the hours after dosing.

MST works because one of the side effects of opiates is constipation, and it works by slowing down the gut.

Because it is an opiate, many doctors do not readily offer MST, so you may have to be persistent to get to use it. For some people it is the only thing that works – and even very low doses mean you can return to a normal life.

Feeling sick (nausea and vomiting)

Most HIV medications include nausea as a potential side effect

Nausea (feeling sick), and vomiting (being sick), is much less common than it used to be, because modern drugs are easier to take. For most people, nausea also improves after a few days or a week as your body gets used to the drugs.

Using an anti-emetic (anti-sickness) pill regularly is often enough. If one anti-emetic does not work, it is worth trying others. Some work by emptying your stomach more quickly and others by stopping the signals that tell your brain that you feel sick.

If the nausea does not improve, there may also be an underlying cause which should be investigated. If it is related to an HIV drug, then you may need to change to another medication.

If you are taking abacavir and you feel like you may be sick or are vomiting, contact your clinic straight away because of the risk of hypersensitivity reaction. *(See page 48).*

How to describe nausea to your doctor

- How often each day do you feel sick, or are you sick?
- How many days a week does this happen?
- How long does the nausea last?
- Has this affected how much you can eat or drink?
- Do you feel more tired or weak as a result?

Medications used for nausea

Domperidone (Motilium): 10-20 mg every 6–8 hours. Suppositories 30-60 mg every 6–8 hours are a good alternative to swallowing pills when you are feeling sick.

Metoclopramide (Maxolon): usually 10mg, 3-times a day. There are slow-release versions, which can be used twice a day, including Maxolon SR and Gastrobin Continuous; however, they should not be used in anyone under 20 years old. Be aware of dystonic reactions (twitching movements) at higher doses.

Prochlorperazine (Stemetil): usually 5–10 mg, 2–3 times daily. A special preparation is available called Buccastem, 1 or 2 tablets are placed between the upper lip and gum and left to dissolve; not having to swallow more pills is useful when you are feeling sick.

Haloperidol: 1.5 mg daily or twice daily where nausea is severe. This is particularly useful as it can be taken at night to avoid early morning nausea.

Sometimes these medications have side effects themselves that you should ask your doctor about.

Where other medications and lifestyle changes have failed and nausea continues, then medications that are normally reserved for patients receiving very strong chemotherapy may be prescribed.

These include granisetron, ondansetron and tropisetron and they are highly effective.

Other suggestions

If changing your medication is not an option and the nausea is continuous, then any of the following suggestions can help.

- Eat smaller meals and snack more frequently rather than eating just a few larger meals
- Try to eat more bland foods and avoid foods that are spicy, greasy or strong smelling
- Leave some dry crackers by your bed and eat one or two of them before getting up in the morning
- Ginger is very helpful and can be used as capsules, ginger root powder or fresh root ginger peeled and steeped in hot water
- If cooking smells bother you, then open the windows while cooking and keep the room well ventilated
- Microwave meals prepare food quickly and with minimum smells, so you can eat a meal as soon as you feel hungry. Getting someone else to prepare your meals can help, if this is possible
- Don't eat in a room that is stuffy or that has lingering cooking smells
- Eat meals at a table rather than lying down and don't lie down immediately after eating

- Try not to drink with your meal or straight after. It is better to wait an hour and then sip the drink slowly
- Try eating cold rather than hot food, or let hot food cool well before you eat it
- Peppermint is also useful and can be taken in tea, sweets or chewing gum
- Acupressure and acupuncture may help, anti-nausea acupressure bands are available from most chemists
- Try to avoid things that irritate the stomach such as alcohol, aspirin and smoking
- If your HIV meds include efavirenz (including Atripla), do not eat high fat meals in the two hours before you take these meds.

Feeling tired (fatigue)

Most HIV medications include fatigue as a potential side effect

Fatigue (feeling tired) used to be reported as a common symptom related to HIV and treatment. It is now reported much less frequently with modern treatment.

Many people instead find they have far more energy, even in the first weeks of treatment, because their viral load is reduced.

Fatigue in HIV positive people is often more likely to be related to other factors than as a side effect of HIV drugs.

These include depression, anxiety, sleep problems, other health complications, and social factors like not having work or enough money.

If your HIV meds stop you sleeping well, you will be tired the next day, so the tiredness can be due poor sleep rather than a direct side effect of the drug.

What is fatigue?

Fatigue is defined as a general feeling of tiredness that does not really go away, even after you have been able to rest.

Fatigue can be physical or mental.

With physical fatigue you are not able to be as active as you used to, even with simple tasks like going up stairs or carrying shopping.

With psychological fatigue, you are not able to concentrate as well as normal or you lose the motivation to do things.

Fatigue can be caused by many things including:

- HIV
- HIV drugs
- Lack of sleep
- Poor diet
- Stress
- Depression
- Antihistamines (used to treat hay fever) and flu and cold remedies
- Alcohol and recreational drug use
- Underlying HIV-related illnesses.
- Being more active than you are able to manage.
- Hormone imbalances such as low levels of testosterone or DHEA (dehydroepiandrosterone) in both men and women.
- Other health conditions

How to describe fatigue to your doctor

Fatigue can start slowly and build up without you realising it. To describe this to your doctor it helps to give examples of when you feel more tired.

If you can compare how you feel now with how you felt six months or a year ago, this will also help.

Describe how often you are tired or out of breath for example. As fatigue can be related to poor sleep, include information about your sleep patterns.

Describe how fatigue affects your daily life.

Lactic acidosis

If you are feeling very tired and have any of the other symptoms associated with lactic acidosis (vomiting, nausea, sometimes pain in the stomach and/or liver, unexplained weight loss, difficulty breathing etc - see page 64) it is very important that you report this to your doctor.

Lactic acidosis is now extremely rare in Western countries and is mainly linked to the early nuke d4T (stavudine).

Treatments

Blood tests can check whether your fatigue is caused by anaemia (low red blood cells). This can be a side effect of AZT and can be treated easily with medication or with a blood transfusion in more serious cases.

You may be feeling more tired because you are not sleeping properly, and one study found this explained fatigue in over 60% of cases. There is more information about difficulties with sleep on pages 36–37.

If you are not eating a balanced diet – ie not getting sufficient calories and nutrients for your body to function normally – this can leave you feeling more tired.

Multivitamins can be prescribed by your doctor, and supplements of vitamin B12 can sometimes help you feel more energetic.

You can also ask to be referred to a dietician who can help you assess and plan changes to your diet.

Psychostimulants like methylphenidate (Ritalin) and pernoline (Cylert) used in low doses, have sometimes been used to treat HIV-related fatigue but side effects include hyperactivity, addiction, loss of appetite and liver toxicity.

Insomnia (not sleeping well)

NOTE: See pages 44–47 for sleep disturbance associated with efavirenz and rilpivirine.

Sleep is an essential part of a healthy life. It is a time when your body is able to rest and repair.

If you are not able to get regular, good quality sleep, either in the long or short term, your ability to think, speak and concentrate will be reduced. You can be irritable and have slower reactions, and your memory and judgement will be affected.

Sleep problems are generally under-reported, under-diagnosed and under-treated. Keeping a sleep diary for the week before you see your doctor can help diagnose some of the problems.

Apart from with efavirenz, insomnia is far more commonly related to depression than a side effect of HIV treatment.

One recent study reported that 1 in 3 HIV positive people had symptoms of depression and in 40% of cases this was not being treated.

Your psychological health relates closely to your physical health. Getting a referral for support for depression, including treatment if appropriate, may help with sleep problems.

Factors affecting sleep include:

- Problems falling asleep at night?
- Waking up too early in the morning?
- Waking throughout the night and only getting intermittent sleep?

Your sleep diary should include when you fall asleep and when you wake up on week days and weekends. Include any naps you have during the day.

- Record how you feel about the general quality of your sleep, including vivid dreaming or nightmares.
- Record drug and alcohol use -– or changes in use such as withdrawal or cutting back on either.
- Caffeine in tea, coffee and cola can affect your ability to sleep, even many hours before you go to bed. Keep a record of how much caffeine you drink during the day and see if changing to a non-caffeine alternative helps.
- Include details about your sleep environment. How comfortable is your bed? Is the room warm and quiet?
- Include when you normally eat. Leaving a couple of hours between your last meal and going to sleep will improve the chance of a better sleep.

Stress and worry can easily disrupt your sleep pattern, as can ongoing health concerns, especially if they are painful or uncomfortable.

Your doctor should also give you a physical check up and blood tests to check for cardiovascular, respiratory or hormonal reasons, especially thyroid function, that may be causing sleep disturbance.

Medication

Sleeping pills are only usually prescribed when other self-help remedies have been tried. They are used to help re-establish a pattern of sleeping. **They are not recommended or generally prescribed for long-term use.**

Sleeping tablets should only be used for a short period and at the lowest dose.

All sleeping pills work in a similar way by reducing brain activity, but the type of sleep they produce varies between different types of drug.

They can help you sleep, but the depressed brain activity means that the quality of sleep is often not as good as natural sleep, and you may still not feel rested the next day.

Sleeping pills reduce the amount of 'dream sleep' that you get which is an important component of good sleep. Sometimes this can leave you feeling drowsy the next day. They can become less effective after even a few days' use, and you can develop a physical or psychological dependency if they are used for more than 1–2 weeks.

Although benzodiazepines (ie temazepam) have relatively few side effects they can interact with protease inhibitors. Non-benzodiazepines such as zopiclone and zolpidem work in a similar way, are shorter acting, and are preferred when anxiety is not a contributing factor.

Melatonin is a hormone produced at night linked to your 'biological clock'. As a supplement it is used to help deal with jet lag and may help return sleep patterns to normal, although side effects include vivid dreams.

Suggestions to help

It is important that the causes of insomnia are diagnosed before any treatment is given.

The wide range of causes mean that non-pharmaceutical approaches, such as having a warm bath or hot milky drink before bedtime, can often make a big difference and are sometimes sufficient.

Do...

- Sleep only enough to be refreshed.
- Get into a routine where you can go to sleep and wake up at the same time each day. Waking up earlier may help.
- Try to exercise every day.
- Avoid extremes of noise or temperature.
- Drink chamomile or other herbal teas.
- Make your bedroom as comfortable and relaxing as possible.
- Eat an evening meal so that you are not hungry when you go to bed.
- Try burning oils.

Don't...

- If you use sleeping pills, don't use them every night
- Drink caffeine drinks or alcohol before bedtime as this will reduce the chance of sleeping well
- Smoke close to bedtime – it makes sleeping difficult
- Try not to nap during the day, so that you are more tired at night when you need to sleep

Mental health

Your mental health describes how you think about yourself and your life on a day-to-day basis. It is about how you interact with your surroundings and the people around you.

From a medical perspective, mental health covers a wide range of symptoms. These include depression and anxiety that can range from mild (which are easy to mange) to moderate and severe (when they dominate your life).

Most people have times when their mental health is fragile. Life involves stress, and stress can change your mood and ability to cope with difficult situations.

If difficulties continue over time, this can increase the risk of other medical problems, including adherence to meds. Getting appropriate help and support is important, and the earlier the better.

You doctor can only help if he or she knows about these difficulties. It is important to say if you are worried.

It is very common for HIV positive people have to have symptoms of depression or mental health problems and these are often untreated.

This can be for several overlapping and complicated reasons.

- An HIV diagnosis affects how you feel about yourself and how you fit in to society. Prejudice is still around–as is ignorance about HIV. This leaves many people feeling more isolated and needing support to restore their confidence about themselves.
- HIV rates are higher in people who are already marginalised or disempowered. This can be related to sexuality, gender, drug use, poverty, sex work, previous abuses and other causes of vulnerability including mental health itself. An HIV diagnosis can further add to this.
- HIV positive people are more likely to use alcohol and recreational drugs which are associated with mental health issues.
- Some HIV drugs have side effects that change your mood and include depression, paranoia, anxiety etc. It is essential that someone with these side effects uses alternative drugs (see pages 44–47).
- HIV can increase the risk of infections in the brain. This is usually related to very low CD4 counts (under 100). Neurological symptoms (how you think, feel and behave due to a direct impact on the brain) have also been reported in very early HIV infection during seroconversion.

HIV and depression

Depression can include a wide range of symptoms and if these continue (for example occuring every day for two weeks) this should prompt referral for a specialist assessment. These include:

- Feeling sad, empty, anxious, restless or irritable in a way that affects your daily life
- Feeling hopeless or pessimistic or that you are not in control of your life
- Lacking energy, or interest in activities that you would normally enjoy
- Feeling guilty, hopeless or worthless
- Having difficulty concentrating, remembering things or making decisions

"After 12 years of treatment I've had my share of difficult side effects but none of them have put me off continuing treatment.

Diarrhoea and insomnia added to my depression, anxiety and agoraphobia. Fatigue from lack of sleep and anxiety have at times made me reclusive. I found psychological side effects are extremely hard to describe or quantify to a doctor.

It is definitely better to ask for help early. Asking for help at a time of crisis might mean a waiting lists to see a counsellor. Anti depressants can help but sometimes have their own side effects."

- Not sleeping or eating properly, weight loss, overeating, lack of interest in personal care
- Thinking about death or suicide or attempting suicide

If you have any of these symptoms, you may be depressed, and your doctor or other heath care workers need to understand how you feel and the impact this is having on your daily life.

Depression can easily be overlooked in general consultations so is often undiagnosed. The earlier you talk about how you feel the easier it will be to get the support you need.

Recovery from depression, even with medications, can take time, but treatment and support can work.

Treatment and management

HIV does not mean you will have mental health problems, but if you are having problems, many things can help.

- Having a friend who you can talk to.
- Support groups reduce isolation and help you meet other people with similar experiences.
- Counselling and/or behavioural therapy can help you cope with issues related to HIV or earlier traumatic experiences.
- Keeping active can keep you occupied. Regular exercise reduces stress and mental health symptoms.
- Medications, such as antidepressants, can reduce symptoms.

Sexual health

Sexual dysfunction, whether due to HIV, side effects of HIV treatments, or other factors, can dramatically reduce quality of life.

Sexual dysfunction includes reduced sex drive (a loss of interest in sex) and physical difficulties (such as loss of erection or difficulty reaching orgasm).

Although several reports linked this to protease inhibitors, sexual dysfunction is not generally reported as a side effect of HIV drugs.

It is likely that sexual problems affect a lot of HIV positive people, not least because of the complex social factors. It takes many people a long time after they are diagnosed before they develop or regain sexual confidence.

Although most research into sexual dysfunction associated with HIV has been carried out in men, when women have been included in these studies, a similar level of concern has been reported.

For example, a study by anonymous questionnaire in over 900 HIV positive people using combination therapy (80% men, 20% women) found that around one-third reported less interest in sex.

With new partners, the decision to discuss HIV, perhaps before you know very much about a person, can be difficult. Not disclosing your HIV status, even when your partner is not at risk because you use condoms, can be a difficult barrier to overcome later in any relationship.

In long-term relationships, fear and concerns about risk may never be discussed or resolved in detail. With an HIV negative partner, either or both partners may become preoccupied with a risk of transmission, however small and however safe their sex. This is a pity given that HIV treatment reduces this risk so low that the impact of PEP (using HIV treatment after a potential exposure) is thought to be minimal if the HIV positive partner has an undetectable viral load.

With HIV positive partners, there can be medical concerns about resistance, reinfection and the risk of other sexually transmitted infections.

Many people find it difficult to talk to their doctor about this aspect of their lives and it is something that doctors rarely ask patients about directly.

Together with many of the medical issues listed below, it may be complicated to identify one single cause.

In 2012, given that treatment has given us the possibility of living a natural life-span, it is important to try and resolve sexual problems. This is something that your clinic can help with, but it is something you may need to be direct and ask about.

Causes

Sexual dysfunction can be caused by a wide range of medical and psychological issues.

- HIV positive men and women have reduced testosterone levels compared to HIV negative people.
- Depression can affect sexual health.
- Many treatments for depression including fluoxetine (Prozac), citalopram (Cipramil), paroxetine (Seroxat) and sertraline (Lustral) can decrease libido and lead to erection difficulties in men. Mirtazapine (Zispin) may be considered as it has little or no effect on sex drive and fewer interactions with HIV drugs.
- Sedatives, tranquillisers and other medications can cause sexual dysfunction, as can smoking, alcohol and recreational/illegal drug use.
- Long-term use of steroids or male hormones.
- Relationship- or work-related stress
- Some side effects are associated with higher rates of sexual dysfunction. This can include neuropathy (for physical reasons) and lipodystrophy (for psychosocial reasons).
- Sexual dysfunction is more common in HIV positive people who are not using HIV drugs compared to HIV negative people.
- Age (older than 40 years), diabetes, pelvic surgery, fear of failure, hypertension can all cause changes in sexual function.

Testosterone levels

If you have a reduced sex drive then ask to have your testosterone levels checked with a simple blood test.

For men, the range for normal levels is 10-30 nmol/L but this does not allow for changes in age. If your levels are lower than this, testosterone replacement treatment can be given by patch, gel, implant or injection.

If you have other symptoms (low sex drive, fatigue, etc) then testosterone treatment is one option you can try, even if you are within ‘normal’ levels.

If your testosterone levels are low, have your bone density monitored as HIV positive people are at higher risk of osteoporosis.

If effective, increased testosterone levels should reduce depression and fatigue and increase sex drive.

Testosterone (at much lower doses) is being studied as a treatment for sexual dysfunction in women. Hair growth, deeper voice and clitoral enlargement are side effects that require caution in women.

Psychological issues

How you feel about yourself and your body and how you feel about HIV can affect your sexual health. HIV negative people and society in general can react in irrational ways to HIV, which can contribute to how you feel as an HIV positive person.

Dealing with an HIV diagnosis, whether or not you are on treatment, takes a lot of courage and perseverance. If treatments work well, you can be faced with new

choices in life and if they are not working well and you are dealing with illness or side effects. You would expect these things to impact on your sex life.

Talk to your doctor. Referral to a sexual health clinic or counselling support is often appropriate. Many clinics have psychologists who are trained and experienced in sexual dysfunction.

Treatments for erectile dysfunction

Different approaches are used depending on the most likely cause.

Approaches to treating erectile dysfunction include counselling, vacuum devices, cockrings and treatments like Muse (an implant) and caverject (an injection).

Oral medications include sildenafil (Viagra), vardenafil (Levitra) and tadalafil (Cialis).

Oral medications can sometimes help reduce psychologically difficult situations. For HIV positive people they should be available on the NHS (after a consultation) or by asking your doctor for a private prescription.

Some HIV medications interact with Viagra. Lower doses – usually one 25 mg in any 48-hour period – are used for people using a PI or NNRTI based combination.

Viagra should never be used with poppers (amyl nitrate).

Viagra is not currently licensed for women although small studies reported benefits.

Section 3:

Drug-specific side effects

CNS side effects: mood alteration, anxiety, dizziness & sleep disturbance

Hypersensitivity reaction (abacavir and others)

Increased bilirubin (yellow skin or eyes)

Kidney toxicity including kidney stones

Liver-related side effects

Latic acidosis, pancreatitis and fatty liver

Peripheral neuropathy

Skin rash

Skin, nail and hair problems

T-20: injection site reactions and other side effects

Lipodystrophy and metabolic changes: fat loss, fat accumulation, glucose and diabetes

CNS side effects: mood alteration, anxiety, dizziness & sleep disturbance

Associated drugs: efavirenz (Sustiva), Atripla (contains efavirenz), rilpivirine (Edurant), Eviplera (contains rilpivirine). Other HIV drugs have also been linked to insomnia or mood changes, though very rarely.

The side effects affecting the central nervous system (CNS) are only associated with efavirenz and rilpivirine (a new NNRTI).

Although case reports of similar side effects have been reported with atazanavir/r, nevirapine, abacavir and other ARVs, these are very rare.

There are several difficult things about these side effects.

Firstly, nearly everyone will get some of these side effects but for most people they will be mild and easy to manage.

This means that you may have some strange dreams, or find yourself daydreaming or getting more worried, or you may get more upset than usual.

Secondly, if you have been told about this before you start treatment, it will be easier to manage and should be less alarming. Information about what to expect before you start taking efavirenz (or rilpivirine) is therefore essential.

CNS side effects can occur after a few hours or after several days and are more common over the first few weeks of treatment. They generally become easier to tolerate.

About a quarter of people in the first efavirenz studies recorded serious CNS side effects. This definition included 'difficulty carrying out daily work'. So although very few people stopped efavirenz in these studies because of the side effects, you have about a 25% chance that it could make it difficult to work as normal until you get used to them.

Starting efavirenz or rilpivirine when you have a few easy days or time of work may reduce any anxiety. It may help if you are more relaxed and less stressed.

Efavirenz may be a difficult drug if you work shifts that require sometimes working days and sometimes working nights. This is becasue most people routinely take efavirenz before they sleep.

Many of the symptoms described here can also be symptoms of HIV-related diseases that are now seen less frequently such as dementia, TB or cryptococcal meningitis. These can develop slowly over time, so describing symptoms to your doctor, in order that they can rule out these factors is very important.

Severe side effects

Some people will experience these side effects much more intensely. If this is the case, it is essential that you get more support as soon as you need it. Perhaps 2-3% of people switch to a different treatment within a few days or weeks.

However, other people only chose to switch after trying efavirenz for several months. This is because although side effects usually get easier to tolerate, they

may continue at a low level for longer than the first few months.

Up to 20% of people may switch over the first year.

CNS side effects can lead to or exaggerate clinical depression, including suicidal feelings and clinical paranoia. It is very important therefore that you are aware that such moods swings can be related to efavirenz and that you are not 'going mad'.

- If you are feeling paranoid and worried about going outside, or have stopped seeing your friends as much, this may be related to efavirenz or rilpivirine side effects.
- Some studies have cautioned against using efavirenz if you are already depressed or have a history of psychiatric illness, but people without such a history have also found symptoms difficult.
- Several reports have been published of severe reactions in people with no previous psychiatric symptoms or illness.
- Some studies have linked higher efavirenz levels to low body weight. Importantly, research in 2004 showed that race may be important. A higher percentage of Africans metabolise efavirenz more slowly. This results in higher doses than needed.
- Often side effects are related to high blood levels of efavirenz. Measuring drug levels with TDM can allow dose reductions without reducing the HIV effect of the combination or risking resistance.

Why these symptoms are associated with efavirenz is not understood. It is also not possible to predict who will experience more severe symptoms.

Reducing CNS side effects

Although you can take efavirenz with or without food, a high fat meal can increase drug levels by 60% and this can increase side effects.

Taking efavirenz a couple of hours before you go to sleep, rather than at bedtime, makes it more likely that you will be asleep when the drug levels are at their highest – about four hours after taking efavirenz.

Haloperidol to reduce anxiety and sleeping pills to help with sleep disturbance may also help, although these have not been formally studied.

If you have difficult side effects with efavirenz and you are not happy with how you feel, then change it for another NNRTI (nevirapine, etravirine) or to a protease inhibitor.

You do not have to continue with efavirenz to prove anything to yourself or your doctor. If you know something is wrong, don't worry about asking to change to something else.

Even if you have only used efavirenz for a few days, if you know it is not for you, it is okay to change. Some drugs are not for everyone.

How to report symptoms

Some of the symptoms associated with efavirenz are not easy to describe.

Writing down the effects you experience will let you see whether they are getting easier.

Sleep disturbance

- Keep a diary of how often your sleep is disrupted.
- Try to describe this in a clear way. Is this every night or several nights a week?
- Can you estimate how much time you sleep each night, and how much you slept in a normal night before you started treatment?

Concentration and memory

- Are you finding it more difficult to concentrate?
- Have you been aware of memory loss recently?

Dreams and nightmares

- How often do you have dreams or nightmares?
- Do these disturb you sufficiently to leave you unsettled the next day?

Mood changes

- If you get mood changes try to describe these clearly in a diary.
- Have your family or friends noticed a change in your behaviour, even if this is not clear to you?

CNS symptoms include:

- Poor concentration, confusion and abnormal thinking.
- Mood swings including anxiety, agitation, depression, paranoia (feeling very anxious or nervous) and euphoria (feeling very happy).
- Disturbed sleep, including insomnia, drowsiness, vivid dreaming and nightmares.

- Examples of how your mood has changed can give a clearer idea of how you are affected.

Depression and feelings of suicide

- A small percentage of people who experience severe side effects have reported feelings of unexplained depression that are out of character, including suicidal thoughts.
- Symptoms at this level mean that it is critical to discuss this with your doctor in order to change to another treatment.
- If you are currently taking efavirenz, you may find it easier to talk to a close friend about how you feel and ask them to come with you for support when you visit your doctor. There is never a problem with taking a friend or family member with you whenever you see your doctor.

"I tried efavirenz but it really was not for me. It was great at getting my viral load reduced, but the side effects were too difficult and I switched to etravirine.

Within days this was like lifting dark clouds and the sun coming out. I didn't realise how much efavirenz was affecting me until I changed it."

Information about what to expect before you start efavirenz is essential.

Some African people clear efavirenz from their bodies more slowly resulting in higher drug levels and risk of side effects.

Although many people use efavirenz without problems, this is a drug that is not for everyone.

Hypersensitivity reactions (abacavir)

Associated drugs: abacavir (Ziagen). Trizivir and Kivexa both contain abacavir.

The main side effect associated with abacavir is a hypersensitivity reaction (HSR) which occurs in around 5% of people. However, a screening test (called HLA-B*5701), reduces this risk to less than 1%.

This test is recommended for all patients in the UK *before* using abacavir.

HSR means that the body is oversensitive to the drug. Hypersensitivity reactions can also occur with nevirapine, T-20, fosamprenavir and cotrimoxazole (Septrin). Genetic tests are only available for abacavir.

Hypersensitivity reaction to abacavir occurs during the first six weeks of therapy in over 90% of cases. Rarely, it can occur much later without any previous symptoms.

You need to know the symptoms of abacavir HSR before starting therapy, even if the B*5701 genetic test indicates a low risk. These include:

- Temperature
- Rash – normally raised and differing in colour from surrounding skin
- Diarrhoea and abdominal pain
- Tiredness and feeling generally unwell
- Nausea and vomiting
- Headache
- Flu-like aches and pains including muscle pain
- Cough and shortness of breath
- Sore throat

These symptoms are general and can be mistaken for many other illnesses including cold, flu and chest infections, especially during the winter period.

It is very important that if you get any of these symptoms after starting abacavir, you see your doctor straight away so that hypersensitivity can be ruled out. A few people who test negative for B*5701 may still get HSR. Even if you tested negative, if you get these symptoms, then contact your doctor.

If these symptoms get progressively worse each day it is an indication that this is HSR. A rash is not always present.

Do not stop taking your medication until you have seen a doctor and a diagnosis of hypersensitivity has been made.

If you stop using abacavir before you have seen a doctor with these symptoms then you will not be able to restart, as hypersensitivity cannot then be ruled out. This means you will be reducing your future treatment options.

If HSR is diagnosed by a doctor then abacavir will be stopped straight away. These symptoms should then disappear very quickly after abacavir is stopped.

Abacavir must never be restarted at any time if you have had the hypersensitivity reaction, as this can prove fatal.

Abacavir is one of the drugs in the combination medicines Trizivir (abacavir+AZT+3TC) and Kivexa (abacavir+3TC)

"I was diagnosed in January 2003 and my viral load was very high and my CD4 count was 60.

When I started my treatment I used efavirenz, tenofovir, 3TC and Septrin. I developed a rash and called my consultant immediately. I was told to go to the clinic and then to stop taking Septrin. So this side effect was from the antibiotic and not the HIV drugs.

I continued taking my ARV's and had restless nights and vivid dreams. After two years my consultant changed my drugs because I was putting on weight.

I take my medication everyday, and the experience I have with these drugs is awesome, I call them good side effects. Why? Because I have a high libido, I become hyper energetic and it has increased my breast size (I know some people don't like that, but it is good for me).

I used to have bad side effects. Now I can proudly say I'm not experiencing them anymore and I'm happy with my meds."

Increased bilirubin, jaundice (yellow skin/eyes)

(Bilirubin is a orange waste product; Hyper = increased; aemia = 'in blood')

Associated drugs: atazanavir (Reyataz); indinavir (Crixivan, rarely used).

An increase in bilirubin (called hyperbilirubinaemia) is a common side effect of atazanavir. More than 50% of people who use this protease inhibitor, especially when boosted by ritonavir, will show increases in a laboratory test.

This is not causing any damage to your body, until levels get higher than five times normal.

These increases are usually mild and less than 10% of people switch to an alternative drug.

When symptoms are noticable, this includes your skin, or the white of the eyes being more yellow. Many people like it because it can looks like a light sun tan.

Indinavir can also increase bilirubin, though this drug is rarely used.

What is bilirubin?

Bilirubin is an orange-yellow part of bile. Bile is the bright green fluid secreted by the liver to help digestion.

Bilirubin is mainly formed by the normal breakdown of haemoglobin (the protein in red blood cells that transport oxygen).

Bilirubin normally passes through the liver. It is then excreted as bile through the intestines.

When this process is interrupted, excess bilirubin stains other body tissues yellow. Fatty tissues like skin, eye tissue and blood vessels are most affected.

Two types of bilirubin

There are two types of bilirubin in the blood.

- Unconjugated (indirect) bilirubin is insoluble in water. This is the bilirubin before it reaches the liver
- Conjugated (direct) bilirubin has been converted to soluble bilirubin in the liver. It then goes into the bile to be stored in the gall bladder or sent to the intestines.

Routine blood tests for total bilirubin measure both unconjugated and conjugated bilirubin.

Increases in bilirubin with atazanavir are of **unconjugated** bilirubin. This is very common with atazanavir.

People who have lower levels of the enzymes responsible for converting bilirubin in the liver will be at a higher risk of increases in bilirubin from atazanavir. This has been linked to genetic factors.

Increases in **conjugated** bilirubin are linked with a range of illnesses and conditions. This includes jaundice associated with hepatitis and cirrhosis, anaemia, Gilbert's disease and sickle cell disease. Jaundice is common in babies. Very high levels in babies can cause permanent damage. Atazanavir is not linked to increases in conjugated bilirubin.

Normal lab levels

Normal values may vary between different labs but are within the following ranges.

Total bilirubin 3 to 17 mmol/L.

Direct bilirubin 0 to 3 mmol/L.

Jaundice only becomes visible at levels above 40 mmol/L. You need good natural light to see this.

Atazanavir doesn't usually need to be changed or the dose changed (of either atazanaivr or ritonavir) unless bilirubin levels increase to five times the upper limit of normal (5xULN). This is at around 60–70 mmol/L.

This yellowish skin can be unusual. When related to atazanavir though it is not causing your body damage.

Less than 10% of people using atazanavir discontinue because of jaundice. If you stop atazanavir, the jaundice reverses within a couple of days.

Using ritonavir as a booster

Just like many other protease inhibitors, atazanavir produces better results when used with ritonavir.

- Ritonavir boosts atazanavir levels by around ten times and makes them more consistent.
- Higher levels of atazanavir at the end of the dose reduces the risk of resistance and may make the drug more active.
- Higher levels also increase the chance of increasing your bilirubin.

Key points

- When related to atazanavir, higher billirubin is not damaging your body
- If this is too disturbing then it often disappears by using higher dose atazanavir without ritonavir
- Check atazanavir levels with TDM.

Individualising dosing

Some people absorb higher levels of atazanavir and may not need the additional boost from ritonavir.

High levels of bilirubin may be a marker of high levels of atazanavir. You can't guess this though–you need to use a test called TDM (see page 19).

In practice, people who get yellow skin or eyes when they use 300 mg/day atazanavir boosted with 100 mg ritonavir are often able to change to unboosted atazanavir (at 400 mg/day). Note that the daily unboosted dose of atazanavir (2 x 200 mg) is a higher dose than the boosted dose (1 x 300 mg capsule).

It is important that your doctor changes the formulation when not using ritonavir.

Atazanavir is available in four strengths: 100, 150, 200 and 300 mg. This enables your dose to be easily adjusted to manage high bilirubin. It is also available as a powder.

Other drugs that affect bilirubin

Other drugs can also increase bilirubin levels. These include anabolic steroids, some antibiotics, anti-malaria drugs, codeine, diuretics, morphine, oral contraceptives, rifampin and sulfonamides.

Drugs that can decrease bilirubin measurements include barbiturates, caffeine and penicillin.

Kidney health and renal side effects

Associated drugs: Drugs cleared by the kidney with potential for renal toxicity include AZT, 3TC, FTC, tenofovir, atazanavir and maraviroc. Truvada, Atripla, Eviplera and Quad all contain tenofovir. Kidney stones can also occur with atazanavir and efavirenz.

The kidney is a major organ that:

- Filters salts and impurities from your blood to be cleared in urine.
- Regulates blood pressure.
- Regulates oxygen levels in blood.
- Helps bone health by processing vitamin D.

Kidney function (also called renal function) can be affected by HIV and other illnesses, including high blood pressure and diabetes.

In someone who has reduced kidney function related to HIV (including HIVAN), this can be improved by starting HIV treatment.

However, several HIV drugs can affect your kidneys and the use and monitoring of these drugs should be managed individually. Kidney function generally reduces as we get older.

Symptoms

Mild kidney disease often has no symptoms, but more advanced kidney symptoms include:

- Nausea and/or vomiting.
- Feeling tired, being short of breath.
- Needing to urinate more often, especially at night, or less often.
- Itchy skin.
- Muscle cramps.
- Loss of appetite.
- Swollen hands or feet (from retaining water) or numbness.

Monitoring kidney function

Routine tests monitor kidney function before and after treatment.

High levels of protein or a waste product called creatinine, indicate that the kidneys may not be working well.

Results from blood and urine tests calculate how well your kidneys are processing creatinine.

Dipstick urine tests

Urine tests can show abnormal levels of protein, blood, white blood cells, glucose and markers for diabetes.

Blood tests

Blood tests can measure protein and creatinine and are used to estimate glomerular filtration rate (eGFR).

eGFR

Estimated GFR is a common way to grade kidney function. It is measured in mL/min per 1.73 m2.

Higher than 90	normal	stage 0/1
60–89	mild	stage 2
30–59	moderate	stage 3
15–29	severe	stage 4
Less than 15	end stage	stage 5

An eGFR less than 60 is defined as Chronic Kidney Disease (CKD).

End Stage Renal Disease (ESRD) inludes preparation for dialysis, transplant etc.

HIV drugs cleared by the kidneys

Several HIV drugs are cleared by the kidney. These include tenofovir, 3TC, FTC, AZT and ddI. The dose for these meds (and maraviroc in some combinations) may need to be changed depending on your eGFR level.

The prescribing information for each drug includes detailed information.

Tenofovir and kidney toxicity

Tenofovir is one of the most widely used HIV drugs and it is mainly processed by the kidneys. Although serious kidney related side effects (including Fanconi's Syndrome) were reported in studies, these were rare. They also often reversed when tenofovir was stopped.

Tenofovir also changes laboratory markers such as reducing creatinine clearance, low phosphate levels and increased protein levels in urine (called proteinuria). The importance of these changes in markers in the long-term is unknown, but it is likely to be more important if you already start with reduced kidney function.

Because tenofovir can also reduce eGFR compared to some other HIV drugs, it is not recommended in people who have eGFR below 75-80 if there are other HIV drugs to chose from.

Similarly, if you are using tenofovir and your eGFR drops to this level, then switching to a different drug is recommended.

If you are using tenofovir, there is a also a caution against using other drugs that are cleared by the kidney.

It is not recommended to use creatinine supplements with tenofovir, as this will affect the interpretation of your monitoring tests.

Kidney stones: atazanavir and efavirenz

There have been several reports of kidney stones that contained high levels of atazanavir or efavirenz, showing that this can be a rare side effect with these drugs.

Kindey stones were also linked to to early protease inhibitor indinavir but this is now rarely used. The side effect of kidney stones was reduced by drinking an additional 1-2 litres of water daily.

Detailed information on kidney stones and indinavir is online.

http://i-base.info/guides/side/kidney-toxicity

Skin problems: rash

Many drugs are associated with rash including: abacavir (Ziagen, Kivexa and Trizivir), FTC (Emtriva), nevirapine (Viramune), efavirenz (Sustiva), etravirine (Intelence), atazanavir (Reyataz), darunavir (Prezista), fosamprenavir (Lexiva/Telzir), tipranavir (Aptivus), raltegravir (Isentress) and T-20 (enfuvirtide, Fuzeon).

Although many drugs are linked to rash, the severity of rash and how long it lasts varies widely.

With some drugs, if you develop a rash during the first few weeks of therapy you must report this immediately to your doctor. This is because it can sometimes lead to very serious reactions.

These drugs are **abacavir** (Ziagen, and in Trizivir and Kivexa), **nevirapine** (Viramune), **efavirenz** (Sustiva), **etravirine** (Intelence), **fosamprenavir** (Lexiva) and **T-20** (enfuvirtide, Fuzeon).

Other rashes are more likely to be mild and disappear without treatment, or can be easily treated with antihistamine drugs such as cetirizine (Zirtek) or loratadine (Clarityn).

Atazanavir can cause a mild rash during the first two months in 10% of people but this disappears without additional treatment within a few weeks.

FTC studies reported rash on the palms of the hands or feet in up to 10% of African Americans, but these have been reported less frequently since the drug has been licensed.

Although antihistamines are available over the counter, it is important that you check with your doctor or pharmacist before taking them, as there can be interactions with HIV drugs.

A rash can also occur as a reaction from exposure to the sun, and will normally resolve. Any rash that makes you feel sick may not be a side effect but a symptom of an underlying disease (such as scabies).

Nevirapine rash with liver toxicity

Nevirapine is linked to two different types of rash. One is the hypersensitivity-type reaction, probably linked to genetic risk factors.

The second is a rash that is related to liver toxicity, and this is more likely to be cause by an immune-related problem, and from starting nevirapine at a high CD4 count. See pages 62–63 on liver toxicity for more details.

Things that can help

- Bath or shower in cool or warm water rather than hot water as this can irritate your rash.
- Avoid heavily scented or coloured soaps and shower gels. Try to use products that are marked hypoallergenic or wash with aqueous cream.
- Use liquids and not powder to wash your clothes as tiny amounts of powder can build up on your clothes. Try using non-biological makes that are designed for sensitive skin.
- Wear cool fibres such as cotton rather than synthetic ones. When possible at home wear as few clothes as possible.
- Try not to use too many bedclothes. Keep as cool as possible in bed as being too warm can irritate your rash. Again, use natural, cool fibres such as cotton.
- Calamine lotion can be soothing when a rash is irritating.

NNRTI rash (nevirapine, efavirenz and etravirine)

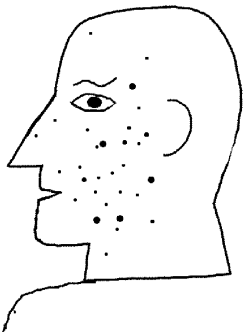
Up to 20% of people using nevirapine, efavirenz or etravirine, can experience a mild to moderate rash in the first weeks of treatment.

For most people this disappears over the next few weeks and they experience no further side effects. Less than 5% of people stop an NNRTI because of rash, and less than 1% people (0.1–0.5%) get a severe (grade 4) rash.

Women are at a higher risk of rash with nevirapine (and perhaps etravirine) than men. Women should not start treatment with nevirapine if their CD4 count is over 250 cells/mm^3 or men if their CD4 count is over 400 cells/mm3.

Nevirapine needs to be dosed in two stages. For the first two weeks, you should only take one 200 mg tablet, once a day. After the first two weeks the dose increases to two 200 mg tablets daily, split into one tablet every 12 hours. The dose should NOT be increased though if there are any symptoms of rash.

If you get a rash with nevirapine, you should make sure your doctor checks this carefully. Everyone starting nevirapine should visit their clinic every two weeks for the first two months to check for liver toxicity (see page 40), so getting a rash examined should be very easy.



Anything more than a mild rash may require stopping nevirapine – but only on the advice of your doctor.

More serious rash (0.3% with nevirapine, 0.1% with efavirenz, less than 0.1% with etravirine) can be life-threatening.

Stevens-Johnson Syndrome (SJS) is a severe hypersensitivity rash and stopping treatment is essential. This is why a rash needs to be seen by a doctor.

Abacavir and rash

A rash can sometimes be one of the symptoms of the hypersensitivity reaction associated with abacavir (also in Ziagen, Kivexa and Trizivir) that occurs in 4-5% of people using abacavir.

It is essential that you see your doctor if a rash appears when using abacavir in a combination.

See pages 48 for more details on this abacavir reaction.

Skin, hair and nail problems

Associated drugs: indinavir (Crixivan, rarely used), 3TC (Epivir), hydroxyurea (Hydrea, rarely used), AZT (Retrovir, nail discolouration) and FTC (Emtriva, skin discolouration)

Problems with hair, nails and dry skin are mainly related to older HIV drugs.

Dry skin

Dry skin, chapped lips and nail problems are a problem for HIV positive people but this is often more related to HIV than HIV drugs.

Indinavir was particularly linked to skin, nail and hair problems. As this drug is now used so rarely, switching to an alternative is the first option.

All the measures listed about rashes are helpful where dry skin is a problem, along with the use of emollients (moisturisers) such as aqueous cream, diprobase, oilatum, and balneum. Try to drink plenty of fluids as well.

Vitamins and a healthy diet are also important for better skin health.

Where rashes and dry skin are unmanageable with medications or simple interventions then ask your doctor to change the medication that is responsible.

You can also ask to be referred to a specialist dermatologist.

Chapped lips have been linked to indinavir in a similar way to dry skin. Regularly using a lip balm and checking indinavir blood levels are both recommended.

Hair loss

People have reported that the thickness and quality of their hair changed while using indinavir – usually becoming thinner – and this has been reported for both head and body hair. Indinavir is rarely used to treat HIV.

Balding patches of head hair, called alopecia, have also been reported, though rarely, with 3TC.

Nail and skin pigment problems

Paronychia (inflammation around the finger nails) and ingrown toe nails have both been reported as rare side effects with indinavir and 3TC.

Many of the people using indinavir are likely to have also used 3TC - so the cause and contribution of each drug is uncertain.

If you are using indinavir consider switching to another drug.

AZT can darken nail and skin pigment in Africans and African-Americans.

FTC (emtricitabine, Emtriva) has been reported to cause pigment changes (mainly to the palms of the hands or soles of the feet) in African people.

FTC is included in Truvada, Atripla, Eviplera and Quad.

Peripheral neuropathy

(peripheral = furthest away; neuro = nerve; pathy = damage)

Associated drugs: ddC (Hivid), d4T (Zerit), ddI (Videx), 3TC (Epivir)

Peripheral neuropathy (PN) is rarely reported with modern HIV drugs.

It was a common side effect from some of the first anti-HIV drugs. It is still is major problem in countries that continue to use d4T (stavudine).

PN can be caused by HIV, especially at low CD4 counts (under 100 cells/mm3). It is also a complication of diabetes, and rates of diabetes are increasing as people living with HIV get older.

It is sometimes difficult to know the cause but if the numbness or pain is symmetrical in both hands or both feet it is more likely to be a side effect than related to HIV.

Symptoms include increased sensitivity or numbness, or tingling in your hands and/or feet. Often it is something you hardly notice, or that comes and goes.

If neuropathy gets worse it can become very painful. It is a side effect that you should take very seriously.

PN is mainly associated with nucleosides, especially the 'd' drugs. These are ddC (no longer manufactured), ddI, d4T and more rarely with 3TC.

Using more than one of these drugs together can increase the risk as can use of other drugs such as hydroxyurea, dapsone, thalidomide, isoniazid and vincristine.

Alcohol, smoking, amphetamines, deficiency of vitamins B12 and E and other illnesses like diabetes and syphilis can also cause and make neuropathy worse; B12 and folate levels can be tested.

Can PN be measured?

Simple tests for neuropathy include comparing ankle to knee reflexes, or using a pin to test sensations from the toes up the leg. A tuning fork will show a reduced vibration in a foot with neuropathy.

Recent studies have measured nerve damage in skin in a biopsy sample.

Your doctor may just rely on what you report is happening. If your symptoms are causing you discomfort or pain, you must make sure it is taken seriously.

Sometimes doctors underestimate how much pain people experience because they think that their patients always exaggerate pain. In fact, most people underestimate pain when talking to their doctor.

Sensitivity tests that measure your reactions to different pressure are not used so frequently, and it can sometimes take 4-6 weeks to get the results. Getting these results recorded regularly though can help you measure any worsening of the symptoms.

pain management clinics include a wide range of treatments and expertise

Is neuropathy reversible?

If you switch treatment early when the side effects are still mild, PN may reverse, but this does not happen for everyone.

Moderate and severe neuropathy very rarely resolves fully but switching drugs can stop the symptoms getting worse. Once established, neuropathy can be irreversible and debilitating.

After switching, you may have to wait several months to know if this helped. Often symptoms get worse before you notice an improvement.

Treatments for neuropathy

There are currently no approved treatments to repair or regrow damaged nerves. One study has shown that acetyl-L-carnitine (Alcar) at a dose of 1500 mg, twice daily, can lead to nerve improvement, but this did not improve pain. Very few clinics in the UK use acetyl-L-carnitine but it can be prescribed on a named-patient basis.

Research into a synthetic human Nerve Growth Factor (hNGF) was stopped many years ago.

Painkillers

Treatments prescribed to manage neuropathy are only used to mask the pain. The side effects of these painkillers can make them difficult to use.

Amitriptyline, nortriptyline (tricyclic antidepressants) and gabapentin and pregabalin (antiepileptic drugs) are used to treatment neuropathic pain.

They do not reduce the pain, but change how your brain perceives it. Even when they help they can be difficult to tolerate because of they also cause drowsiness.

Opiate-based painkillers such as codeine, dihydrocodeine, fentanyl, methadone, morphine and tramadol sometimes help when the pain is severe.

Although not always appropriate for neurological damage, they sometimes help. It can take several days to find the appropriate dose, and these drugs can interact with some HIV drugs. A side effect of opiates is constipation.

Cannabis (marijuana), or synthetic versions such as nabilone (Cesamet) or dronabinol (Marinol) reduce pain related to neuropathy. They can be prescribed in the UK.

Capsaicin patches that contain chilli pepper are available in the UK.

You should also have appropriate care from a pain control nurse specialist, rather than your HIV doctor. They will be able to make a full assessment of your level of pain, and adequately prescribe medication to reduce it.

More rarely, when pain is so great that it is not treatable, alcohol can be injected into a nerve junction. Nerve blocks can be very effective when they work, and are a specialist procedure, but can also cause loss of sensation and sometimes produce unpredictable results.

Other treatment approaches are listed on the next page, though there is limited research to support some of these.

Alternatives to painkillers?

Alternative options may be a more acceptable and effective way to manage neuropathy.

Although not always proven in studies, there is anecdotal reports on these approaches. With a condition that is painful, it is worth trying each of these in case they help (though not all at the same time).

Acetyl-L-carnitine (Alcar) is a supplement that has been effective in small studies and anecdotally. Other studies did not find a benefit.

Acupuncture is annecdotally reported to improve quality of life but not supported by research. A study comparing acupuncture to placebo showed no benefit, but the acupuncture was a standardised rather than individualised treatment. This is one you need to decide for yourself.

Magnets – Using magnetic insoles have reported benefits in diabetic-related neuropathy, although a published study found little difference compared to placebo (sham) insoles.

Local anaesthetic creams such as Lidocaine (5%), and Lidocaine patches reported benefits in recent studies.

Capsaicin – Patches made from chilli peppers that causes increased local blood flow when applied to the skin. Although approved in Europe the FDA in the US did not approve the Qutenza patch for HIV neuropathy. This was because the studies did not show a clear benefit.

Voltarol (NSAID) – a nonsteroidal anti-inflammatory drug.

Alpha-Lipoic Acid – 600 to 900mg daily may help protect nerves from inflammation.

Cod liver oil – One or two tablespoons a day has anecdotally produced beneficial reports, especially if the symptoms have not become very severe. This is not as bad as it sounds as modern oils are palatable and also come in flavours.

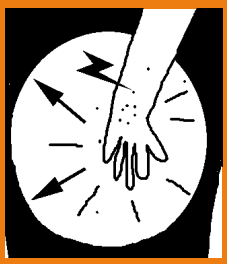
Topical aspirin – suggested in one recent study that aspirin, crushed and dissolved in water or gel and applied to the painful area can relieve symptoms.

Vitamin B6 (pyridoxine) – requires caution with dosing as B6 can also worsen neuropathy (100mg daily is sometimes recommended).

Vitamin B12 – available as injections, lozenges, or nose-gel. B12 levels should be checked by your doctor. Dosage varies but if levels are too high this can worsen neuropathy.

Magnesium – 250mg – 2 capsules each morning

Calcium – 300mg – 2 capsules each evening



Other suggestions

- Avoid tight fitting shoes and socks which restrict blood circulation.
- Keep your feet uncovered at night - keeping them cooler and out of contact with sheets or bedding.
- Try deep tissue massage.
- Don't walk or stand for long periods.
- Soak your feet in cool water.

Further reading:

Useful recommended reference books written in non-technical language are *Numb Toes and Aching Soles* (July 1999) and *Numb Toes and Other Woes* (July 2001) both by John A. Senneff. ISBN: 0967110718 and 0967110734.

Lark Lands has led community-based research in the use of nutrients, diet and supplements for PN. This comprehensive overview is recommended:

http://www.larklands.net/TR12_Neuropathy-Nutrients.PDF

http://www.larrylands.com/lark/larktreatments.htm

Neuropathy Trust (UK) offer information and support:

http://www.neurocentre.com

Neuropathy Association (US):

http://www.neuropathy.org

Neuropathy can be very painful and debilitating... ask for a referral to a pain management clinic...

Management summary:

- Change HIV drug(s) that are responsible
- Acetyl-L-carnitine (Alcar)
- Cod liver oil
- Painkillers such as gabapentin, amitriptyline or nortriptyline (or marujuana) may mask symptoms
- Referral to a pain management clinic is important and can access a wider range of treatments

Liver-related side effects

Associated drugs: nevirapine (Viramune), ritonavir (Norvir), tipranavir (Aptivus).

Most anti-HIV drugs have potential for liver toxicity.

Your liver is generally a strong organ. Its job is to filter chemicals from your blood. It usually does this very well.

A lot of people worry about the perceived damage that medications can have on the liver. Most drugs however, including HIV drugs, are actually easily filtered without causing problems.

But routine blood tests will check your liver enzymes (ALT and AST). Liver toxicity becomes a more complicated problem when alcohol use or viral hepatitis have damaged the liver.

A few HIV drugs, including nevirapine, have been linked to liver problems. If this is the case, then the information leaflet that comes with your meds includes a 'black box' warning. Liver toxicity has also been reported with efavirenz. Ritonavir and tipranavir (due to the higher ritonavir dose) are also linked to liver toxicity.

The following factors can increase the risk of liver complications from HIV treatment.

- Viral hepatitis: hepatitis A, B or C (or other liver disease).
- Increased alcohol consumption.
- Use of other drugs, including recreational drugs, that are toxic to the liver.
- Gender: women are more prone to liver problems with HIV drugs.

Your doctor will normally test your liver function at the same time as testing CD4 count and viral load.

If you have hepatitis or previous liver damage, therapeutic drug monitoring (TDM) should be used if you are using protease inhibitors or NNRTIs, you may need to use a lower dose.

When taking anti-HIV drugs you should report any side effects to your doctor. Especially if you have abdominal pain, nausea and vomiting, yellowing of the skin or the whites of the eyes.

Where liver toxicity is suspected, the drugs will normally be stopped to allow the liver to rest and return to normal. When the liver tests have returned to normal HIV drugs may be restarted. This is often with a different combination of drugs or reduced doses.

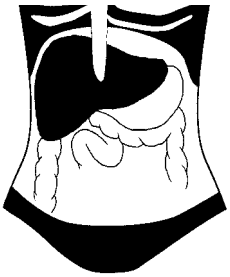
Nevirapine

The risk of nevirapine-related liver toxicity is different between men and women. This risk is related to CD4 count when starting treatment.

Women starting treatment for the first time should not use nevirapine if their CD4 count is over 250 cells/mm^3 and men should not use nevirapine if their CD4 count is over 400 cells/mm^3.

These CD4 upper limits are not thought important if you already have an undetectable viral load and are switching one of your current drugs to nevirapine. They do not relate to pregnant women who are using a single dose of nevirapine as part of treatment to reduce the risk of transmitting HIV to their baby.

Close monitoring (every two weeks) in the first two months of therapy is recommended for anyone who starts a nevirapine-based combination. This is when liver problems first start to occur. Liver toxicity may also build up slowly and



so routine monitoring after the first two months is also important.

Nevirapine must be taken as one tablet (200mg) ***once*** daily for the first two weeks.

Only if you have none of the symptoms listed below and your liver function tests are within the acceptable levels can you increase your nevirapine dose to one tablet (200mg) ***twice*** a day.

Blood samples should be taken every two weeks in the first two months to check liver function, then at the end of the third month, and then every three to four months if they are within normal limits.

During this first eight weeks you should contact your doctor straight away if you have any of the following symptoms:

- Rash
- Blistering of the skin – seek immediate medical attention
- Mouth sores
- Facial or general swelling
- Fever
- Flu-like symptoms, aching muscles or joint pains

Your doctor will do another liver function blood test if you have one of these symptoms.

If the results are not higher than twice the normal limit, and depending on the severity of your symptoms, a decision will be made whether or not to continue with nevirapine. If a decision is made to continue, you will be very closely monitored to ensure that the symptoms do not progress or your liver function tests get worse.

If your liver tests get to five times the normal limit or mild symptoms get worse, then your nevirapine must be stopped. Your doctor will recommend whether you need to stop all your treatments or just switch the nevirapine to another drug.

If you stop nevirapine for these reasons, you must not take it again in the future.

Hepatic steatosis/fatty liver

Hepatic steatosis is a medical term for 'fatty liver'. This can develop from alcohol use, hepatitis, obesity and drug toxicity with the family of HIV drugs called NRTIs (nukes).

This build-up of fat in the liver can affect the way it processes fats. Hepatic steatosis often also leads to lactic acidosis (see page 64). People who weigh over 70 kgs, especially women, may be more at risk of developing hepatic steatosis and lactic acidosis.

Ultrasonography is a sensitive, accurate, non-invasive screening tool to detect steatosis as this is not always shown in liver function tests.

Steatosis is also common in HIV positive children. It has no impact on disease, testing or management.

Lactic acidosis and pancreatitis

All nukes (d4T, ddI, abacavir, tenofovir, FTC, 3TC, AZT), hydroxyurea and ribavirin, have been linked to reports of lactic acidosis and/or pancreatitis. PIs and efavirenz have also been associated with pancreatitis.

Lactic acidosis

Lactic acidosis is a very serious side effect that has almost disappeared from countries that no longer use d4T, ddI and AZT. Although other nukes are linked to lactic acidosis one or both of these nukes are linked to most cases.

Symptoms include:

- Unexplained tiredness, often severe.
- Sickness (vomiting) and nausea.
- Pain in the stomach, abdomen and/or liver.
- Unexplained weight loss.
- Difficulty breathing.
- Poor blood circulation – cold hands or feet or bluish skin colour.
- Sudden peripheral neuropathy.

Treatment and monitoring

Early diagnosis is essential – and contacting your doctor if you have any of the symptoms is important. HIV treatments may need to be stopped immediately depending on blood levels.

More info

More detailed information on lactic acidosis is included online.

http://i-base.info/guides/side/lactic-acidosis-pancreatitis

This includes a 6-page leaflet with information on how to minimise ISRs and tips for how to mange other aspects of an injectable treatment.

Pancreatitis

The pancreas is the organ that produces enzymes to help the digestion of food in the stomach. It also helps regulate insulin which controls the levels of sugar in your body.

Pancreatitis means inflammation of the pancreas.

It an uncommon or rare side effect of some HIV drugs including 3TC, d4T, ddI, hydroxyurea (rarely used) and is a very rare side effect of Septrin.

It can also be caused by gallstones, excess alcohol, other medications or infections.

Triglycerides higher than 10 mmol/L, increases the risk of pancreatitis and needs to be promtly managed. Pancreatitis can still occur when triglycerides are 5-10 mmol/L.

Pancreatitis can also be hereditary (genetic).

Symptoms and diagnosis

Symptoms include upper abdominal pain with severe nausea and vomiting.

Blood tests measuring amylase lipase are usually checked to confirm a diagnosis of pancreatitis.

Measuring faecal amylase (FE1) shows whether pancreatic enzymes need to be supplemented.

Pancreatitis can be fatal if not treated early. If it is a side effect of HIV drugs, these medications need to be changed.

T-20: injection site reactions (ISRs) and other side effects

Associated drugs: T-20 (enfuvirtide, Fuzeon)

T-20 was approved in 2003 in Europe and was the first entry inhibitor. This type of drug works against HIV before it gets inside a CD4 cell.

T-20 is a more complicated treatment because it is not an oral drug. T-20 is given by subcutaneous injection, twice-daily. These are injections under the skin, not into a vein or muscle.

However, if you need to use T-20 as a life-saving drug, it will work against other drug resistant virus. As with any drug, it needs to be used in combination with other active drugs.

In 2012, very few people are still using T-20. This is because newer drugs, including raltegravir, darunavir and etravrine, also work against drug resistant HIV.

People who used T-20 successfully as a life saving treatment have usually been able to switch safely to these newer drugs, which are generally easier to take.

If resistance develops to the newer drugs though, T-20 is still an important option.

The main side effects from T-20 include injection site reactions. Other side effects include bacterial pneumonia, hypersensitivity reactions, and mood changes (euphoria).

Online information

More detailed information on T-20 is included online.

http://i-base.info/guides/side/t-20

This includes a 6-page leaflet with information on how to minimise ISRs and tips for how to mange other aspects of an injectable treatment.

Lipodystrophy and metabolic changes

(lipid = fat; dystrophy = disorder)

Lipodystrophy is a medical term referring to changes in body fat.

When this is part of a set of symptoms related to HIV treatment, it is usually linked to other metabolic changes.

The word 'metabolic' refers to how your body processes food into energy. This includes the production, regulation and storage of fats and sugars.

Although doctors are now aware of lipodystrophy as a side effect, you may still have to take an active role in getting the best monitoring and care.

The mechanism that causes fat loss is now understood. Hopefully, over the next few years, research will discover the cause(s) of metabolic fat gain.

What are the symptoms?

There are three broad sets of lipodystrophy symptoms:

- Fat loss (from legs and arms leaving veins more prominent, also from buttocks and the face).
- Fat gain (in the stomach, breasts in both women and men, shoulders, neck and sometimes small lumps of fat under the skin (called lipoma).
- Metabolic changes that affect the way your body produces and processes fats and sugars.

Any information about lipodystrophy needs to specify which of these symptoms are being discussed.

Each symptom is thought to have a different mechanism. You can have one symptom without the others.

Even when symptoms are generally linked to one class of drug, the effect of each drug can be very different.

Lipodystrophy is likely to be the result of several different factors rather than any single cause.

These include your HIV treatment history, individual drugs, lowest CD4 count, age, diet, exercise and family health.

These changes have been reported in men, women and children from a wide range of racial backgrounds.

How many people are affected?

Many people are unlikely to notice any changes in body shape. Lipodystrophy occurs more rarely with current drugs compared to the earliest HIV meds.

The benefits from treatment still outweigh the risks. For most people any changes are likely to be mild. However, for a minority, problems are more serious.

Preventing lipodystophy is more important and more successful than trying to treat lipodystophy after it has developed.

As no one can predict who will be affected before starting treatment, careful monitoring is important. You use try switching to other HIV meds if you get symptoms with your first combination.

Monitoring changes in fat distribution

There are several ways that changes in body fat distribution can be measured and monitored.

- Most people are sensitive to physical changes in their body. This means that 'self-reporting', perhaps with careful measuring by a dietician, or photography can record any changes.
- Some HIV clinics have access to scanning equipment, but unfortunately lipodystrophy is rarely monitored in this way. MRI and DEXA scans look at the breakdown within your body of fat and muscle. A test called BIA (Bio Impedance Analysis) are sometimes used. (See side box on Monitoring Tests).
- Getting a DEXA scan, or well-lit photo, even if you only have slight changes, will give you a reference to know how quickly symptoms are progressing or improving. Some specialist clinics, including the lipodystrophy clinic at St Thomas' Hospital in London, provide baseline DEXA scans to all patients. You can self refer to this clinic.
- As with your CD4 and viral load results, a single test result may only provide limited information. You are likely to need several tests over time to monitor changes.

If you are worried that you have lipodystrophy, make sure this is taken seriously. You should be offered monitoring and have any treatment choices explained.

Changing treatment

Changing treatment can sometimes reverse fat loss, see pages 70–72.

Studies to reverse metabolic fat gain, had less success, see pages 74–75.

but just because studies haven't shown a benefit, it doesn't mean that another treatments will not be better for you. Whether you decide to change treatment will depend on:

- Your treatment history, and
- How badly the lipodystrophy is affecting you.

Any new combination will need to be just as effective against HIV.

Using combinations without nucleosides is one new strategy that is being studied. Another might be to use an entry inhibitor or integrase inhibitor instead of a PI or NNRTI.

Switching to drugs that have less impact on blood lipids can help with cholesterol and triglycerides,

It will be much easier to know if the switch has worked if you have been monitored before you make any change.

Even if this does not reverse the symptoms, changing to a different drug or combination may stop the symptoms getting worse.

Monitoring tests

The following tests can monitor changes. Having a measurement before starting treatment will make it easier to interpret any change.

Measurement: careful measurement by a dietician using callipers can be useful if nothing else is available. This may be useful for fat increases but will be less sensitive for fat loss. Results may vary depending on the dietician. Measurement by callipers is not sensitive for small changes. Waist circumference (over 102 cm for men and 88 cm in women) and waist:hip ratio (higher than 0.95 in men and 0.90 in women) are also used.

DEXA (or DXA) scan (Dual X-ray Absorptiometry)**:** these scans are available at most main hospitals as they are routinely used for checking bone changes as people get older. You lay on a flatbed scanner for 5–20 minutes (depending on the scanner) for a full body scan. Your head is not scanned. The results provide a breakdown of your body composition into fat, bone and muscle. Some doctors would like a DEXA scan before any HIV treatment is started, and repeated annually to monitor for changes.

DEXA scans can show the percentage of body fat in each main section of your body - in each arm, leg, your head and your trunk. An important limitation is that DEXA scans cannot show whether trunk fat is visceral (around the organs inside your abdomen) or subcutaneous (love handles - under the skin but outside the abdomen). Visceral fat is most associated with HIV-related fat accumulation.

MRI scan (Magnetic Resonance Imaging)**:** these scans are much less readily available and the equipment required is more sophisticated and expensive. An MRI scan provides a computer image of the tissues, muscle and bone in a cross-section of any part of your body. An MRI scan can show how fat is distributed – whether it is subcutaneous (under the skin) or visceral (around your central organs) – and is very accurate at measuring any changes.

Bio-electrical Impedance Analysis (BIA):

BIA is a simple painless procedure that calculates the percentages of fat, muscle and water in the body according to height, weight, sex and age.

It has mainly been used for HIV-related wasting but may also be useful in monitoring lipodystrophy.

Weight in people with lipodystrophy is generally stable. Fat redistribution (rather than weight gain or loss) is usually the issue. However, weighing yourself is important in case you have lost or gained weight without realising it.

Fat loss (lipoatrophy)

Associated drugs: d4T (stavudine), AZT (zidovudine, Retrovir), possibly efavirenz (Sustiva).

Symptoms

Lipoatrophy is the medical term for fat loss. Some researchers see this as the main symptom of HIV-related lipodystrophy.

Symptoms include loss of fat from under the skin on your arms and legs, which can make your veins look more prominent. It also includes loss from the face, especially sunken cheeks and temples.

Fat can be lost from the soles of the feet making walking more painful and tiring.

Role of d4T and AZT

Clinical lipoatrophy - where you can see a change in body fat - is common after using either d4T or AZT for more than six months. Both drugs affect the way that fat cells are produced and develop.

At a cellular level this can occur after only a few weeks or months of treatment.

Nucleosides (nukes) have been shown to damage the energy producing part of healthy cells called mitochondria.

In most studies, d4T damages fat cells at around twice the rate compared to AZT. d4T may also lead to lipoatrophy that is more difficult to reverse because it may damage cells at an earlier stage of their development.

Other nukes?

Not all nukes cause lipoatrophy. This is not a side effect of 3TC, FTC, tenofovir and abacavir. The role of ddI is unclear.

The risk of lipoatrophy for people who are starting their first treatment should now be very low in Western countries. Newer drugs do not cause this side effect, and increased monitoring should pick this up if you are using older drugs like AZT.

Neither d4T or AZT are recommended as routine first-line therapy in the UK, unless specific health complications require it. People currently using either of these drugs should be offered alternatives.

Other HIV drugs and fat loss

Some studies reported a higher risk of fat loss when d4T or AZT were used with protease inhibitors.

The US study ACTG 5142 reported higher rates of fat loss in people using efavirenz compared to lopinavir/r, even when use of nucleosides were taken into account. These findings are not fully understood.

Several studies have reported higher rates of lipodystrophy in people using combinations that include three drug classes–nukes, NNRTIs and PIs.

Switching treatment

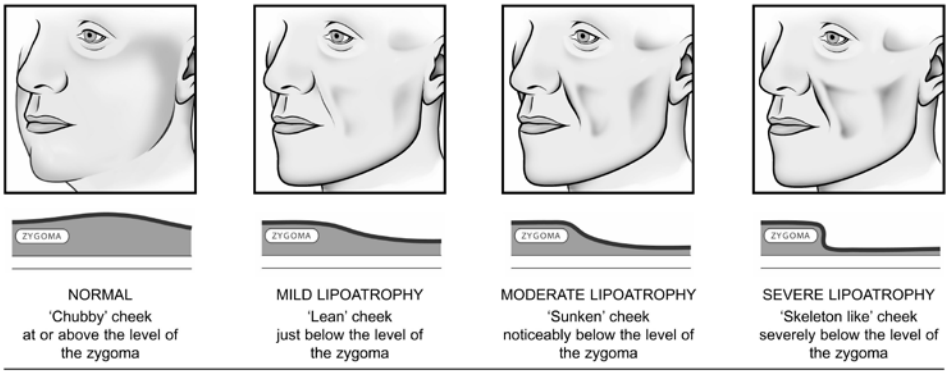
Switching d4T or AZT to either abacavir or tenofovir, or using other combinations of drugs, can reverse the fat lost in limbs.

Reversing fat loss from the face or buttocks is more difficult, but this may be possible if you switch treatment early.

Switching is very safe, but the choice of new drugs needs to consider your previous treatment history to minimise the risk of drug resistance.

Any reversal of the fat loss is likely to take at least six months to become noticeable. This is because these symptoms

Figure 3: Visual scale to grade HIV-related facial lipoatrophy



Note: Zygoma = cheekbone. Source: St Stephens AIDS Trust, Chelsea and Westminster Hospital

developed slowly and if they are going to reverse this will also take time.

In studies where people switch, approximately +0.3 kg can be detected by scans at 6 months. In one study it took about two years (with an increase of +1.3 kg) before these patients noticed a difference.

Injectable treatments

Many substances have been used to treat HIV-related fat loss in the face but very few have been carefully researched. Many of these are used without approval for treating HIV-related fat loss.

Although non-permanent products need top-up treatment, these are currently the safest option. They work with your natural ageing process. Unlike permanent implants, there is no risk of it moving.

In the US, only New-Fill and Radiesse have been approved to treat HIV-related facial lipoatrophy.

In the UK, New-Fill is the most widely used, and as it is approved by some NHS trusts, we focus on this product in this guide. It is also supported by the strongest safety and efficacy results.

New-Fill (Sculptra)

New-Fill (polylactic acid, PLA) has shown promising results in correcting the effect of facial fat loss and is approved in the US as a treatment for HIV-related lipoatrophy. Most people require 4-5 sets of injections but severe cases may require more sessions.

New-Fill does not replace fat but generates new collagen growth. This gives the effect that your skin grows thicker, sometimes by up to 1cm. This process continues for several months after the injections have finished.

New-Fill has also been used to correct fat lost on the soles of the feet.

New-Fill is available free on the NHS in many of the larger HIV clinics in the UK. These include Brighton, Manchester, and any patient attending a London clinic. Since 2005, New-Fill has been available free on the NHS for any patient registered at a London clinic.

UK HIV treatment guidelines recommend that corrective treatment or surgery should be provided on the NHS.

Further info: a US community site with information on lipoatrophy

www.facialwasting.org

However, New-Fill is not equally available throughout the UK. You may have to lobby you doctor and NHS trust. You may decide to register at a new HIV clinic to access this treatment.

Private treatment costs vary by clinic. Private treatment should ONLY be from a practitioner with experience treating HIV-related lipoatrophy.

Other injectible compounds

Radiesse

A second non-permanent filler approved in the US to treat HIV-related facial fat loss is called Radiesse. This is the trade name for a formulation of calcium hydroxylapatite suspended in a gel.

Although this is used in some private clinics in the UK, it is not approved by the London commissioners as a free NHS treatment.

Bio-Alcamid

Bio-Alcamid (polyalkylimide, Polymekon) is a 'gore-tex' filler that was used briefly but has now been linked to serious complications in 10% people. These relate to infections in the implant, often years after the procedure.

BioAlcamid no longer being used or recommended in many countries including the UK.

Although the manufacturer claims that BioAlcamid can be removed, it is a permanent implant because removal is traumatic and becomes increasingly difficult over time.

Anyone who has used BioAlcamid should inform their dentist about their implants and not have dental injections close to the implant site.

Other complications have been reported from trauma. Do not take up boxing or contact sports.

BioAlcamid has probably been used by several hundred people in the UK, and several thousand people in Europe and the US. Information is difficult to assess because this was largely in private clinics.

Silicone

Other approaches try to inject or implant material (fat or silicone) and hope it will stay in position. Very often, it disperses, moves or appears lumpy.

Silicone injections are dangerous and ineffective and were banned in the US many years ago.

A fine grade formulation called Silikon 1000 Microdroplets was studied in the US but further results were not available when updating this guide.

Fat transfer (Coleman technique)

Fat transfer involves extracting fat from one body site and reinjecting it surgically in another. This is usually subcutaneous fat from the stomach, which is then transplanted to the face.

Fat related to lipodystophy (ie shoulder fat) should not be transplanted.

Although results are very good the process is now less frequently used. This is because it is involves invasive, traumatic and expensive surgery.

"I was very worried about the fat accumulation in my abdomen. Not only because of my physical appearance but also because the pressure from inside and the feeling of being full were very unpleasant.

I decided to do something about it. I looked for information at an AIDS organisation, then I talked to my doctor.

I changed treatment, and my diet - more fruit and veg. Aerobic exercise really helped. Swimming and cycling are my favorite activities.

I have started to feel better and I'm happier when I see myself in the mirror."

Fat accumulation

Associated drugs: nukes, NNRTIs, protease inhibitors, possibly integrase inhibitors

Symptoms

Fat accumulation can occur in the abdomen, breasts, neck and shoulders. It can occur in both men and women. Small bumps or collections of fat, called lipomas, can occur under the skin in other parts of the body including the pubis. A hard fatty lump in a mans breast is called gynaecomastia.

Abdominal fat can be *visceral* or *subcutaneous.* Visceral adipose tissue (VAT) is fat that is around the organs inside the abdomen. Subcutaneous adipose tisue (SAT) is fat under your skin ('love handles').

With visceral fat your stomach wall is pushed out from inside. Your stomach muscles can sometimes be quite defined, but your stomach will still be extended.

In severe cases, this can compress your internal organs and interfere with normal functions like breathing and eating.

In these cases there is a greater medical urgency to reverse the fat accumulation. This may help you access treatments like growth hormone releasing factor (GHRF, tesamorelin), growth hormone (rHGH) or to switch to drugs like T-20 or raltegravir.

Treatments for fat accumulation

Diet, exercise and some treatments may help. Using more than one approach may be important. For example, using diet and exercise in addition to anthing else that you try.

Diet means having a healthy balanced diet. It does not mean you should dramtically cut calorie intake, which makes fat loss more difficult.

HIV-related fat accumulation seems to be due to your body signalling itself to produce more fat. **Dietary fat** is not the only mechanism, but high fat diets are unlikely to help. Whatever the cause, **diet and exercise** seem to be useful in helping reverse these changes.

Anabolic steroids are **not** recommended for fat accumulation as they could worsen fat loss in other parts of the body.

Metformin can reduce central fat accumulation in people who already have insulin resistance but should not be used if you have a low BMI.

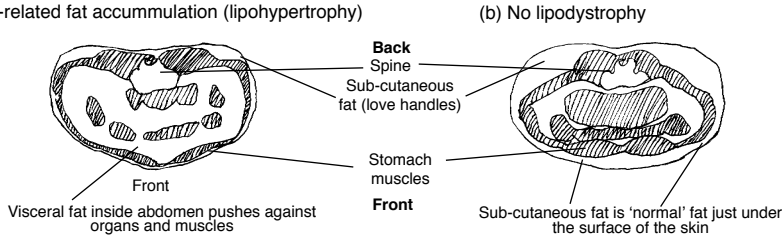
Recombinant Human Growth Hormone (rHGH) can reduce visceral abdominal fat and fat pads from the back of the neck and shoulders. Side effects, including the risk of insulin resistance and diabetes, are reduced using lower doses in more recent studies. Fat accumulation appears to return if rHGH is stopped.

A Growth Hormone Releasing Factor called **tesamorelin** (formerly TH-9507, tradename Egrifta) that can reduce visceral fat by 20% was approved in the US in 2010. It had less side effects than rHGH but there is no long-term data (maximum one year).

Tesamorelin is a continual treatment and fat returns if the treatment is stopped. A lower maintenance dose of tesamorelin has not been established.

Neither tesamorelin nor rHGH are approved in Europe as treatments for lipodystrophy. However, rHGH can be prescribed off-label on an individual patient basis. Tesamorelin is unlikely to be approved in Europe in the near future.

Figure 4: Illustration of MRI scans, fat shows as white areas



Neck, shoulders, breasts and lipomas

Removing fat from the neck or shoulders using liposuction has worked well for some people. The results were sustained in 50% of people but fat returned after several months in 25-50% of people.

There may be a higher likelihood of a permanent result if at the same time, HIV treatment is modified and diet and exercise changed.

Unless the underlying metabolic mechanism is altered, fat accumulation may return after several months.

Liposuction cannot be used for visceral fat accumulation in the abdomen.

Anecdotally, testosterone cream massaged onto the fat pads reduced fat pads on the shoulders. A lower dose should be used for women than for men.

Liposuction and surgery are also used to reduce breast size in both men and women.

Breast lumps (gynaecomastia) in men has been mainly linked to efavirenz, so switching treatment is a first option. Dihydrotestosterone gel (Andractim) may help.

Women with lipodystrophy may have higher levels of testosterone than either HIV positive women without lipodystrophy or HIV negative women. It is not clear whether this is due to high insulin levels associated with lipodystrophy, although a link between the length of time on PI-therapy (but not other drugs) and a greater chance of higher testosterone was found in one study.

Switching HIV drugs

Studies switching individual drugs have been less helpful with fat accumulation than with fat loss. In theory, if one particular drug is linked to these body changes then it is very reasonable to at least try another one, in case this works for you.

If you change your combination, you have to change it to one that is just as effective against HIV.

There have been anecdotal reports and case studies of people whose shoulder and/or abdominal fat decreased after switching to atazanavir. A general benefit was not seen in a larger study.

Fat accumulation does not seem closely related to high blood lipids. So far, newer drugs that affect lipids less (unboosted atazanavir, nevirapine, raltegravir and T-20, maraviroc) have not shown reduced rates of fat accumulation.

Cholesterol and triglycerides

Cholesterol and triglycerides are two types of fats that are carried in blood. These fats perform essential functions, including making effective cell structures and processing vitamins A, D, E and K.

Cholesterol and trigylcerides are often referred to as 'lipids'.

When levels are too high, this increases the risk of heart disease and stroke in the general population.

However, if this is a side effect of treatment for a short time, there may be differences to the general population where abnormal lipids are often increased and sustained for many years or decades.

HIV and lipids

HIV itself (before treatment) reduces both good and bad cholesterol and triglycerides are higher. Starting treatment with any combination will reverse these lipid effects as part of a return-to-health effect.

Because many HIV drugs and lifestyle factors affect lipids this is complex to interpet.

Testing and monitoring

Cholesterol and triglycerides should be checked when you are first diagnosed. They should also be tested before starting or changing treatment and then three months after any change.

Routine monitoring for someone on stable treatment should then involve checking lipids every 6–12 months.

Most clinics will do this at the same time as your CD4 and viral load, but you may need to ask whether this is being done. These tests are best done fasted (on an empty stomach) so don't eat or drink anything before your have your blood taken on those days.

Management of lipid levels should be part of an assessment of your risk for heart disease. This is also related to other risk factors, including lifestyle factors.

Lipids are first managed by diet and exercise, then by switching HIV treatment and then by using lipid lowering drugs.

Cholesterol

Total cholesterol (TC) is measured first. If these results are high then a further test will break this down into two different types of cholesterol:

i) High Density Lipoprotein (HDL) is 'good' cholesterol. It removes fats from your arteries.

ii) Low Density Lipoprotein (LDL) is 'bad' cholesterol. It is a small molecule that carries fats from the liver to other parts of your body and can lead to heart disease.

Target levels for total and LDL cholesterol and desirable levels for HDL cholesterol and triglycerides are shown in Table 5. Target levels are lower for people who already have high cardiovascular risk due to other factors. Each 1.0 reduction in LDL reduces CVD mortality by 20%.

The TC:HDL ratio is used to determine the importance of using lipid lowering drugs, but is not used for monitoring afterwards.

If triglycerides are high, the test for HDL and LDL is more difficult to run.

Table 5: Target/desirable levels for fasted lipids (EACS guidelines)

Total cholesterol	Less than 5.0 mmol/L (under 4.0 if high risk)
LDL cholesterol	Less than 3.0 mmol/L (under 2.0 if high risk)
HDL cholesterol	Higher than 0.9 mmol/L
Triglycerides	Less than 1.7 mmol/L

Table 6: Factors that can affect cholesterol and triglycerides

HIV	TC is lower and TG is higher before HIV treatment
HIV treatment	Some drugs affect cholesterol (LDL and HDL) and TG
Ageing	Ageing can increase cholesterol and TG
Smoking	Increases LDL. Quitting increases HDL and reduces TG
Diet	Diet affects blood lipids
Exercise	Exercise has a good impact on lipids
Other infections	Other health conditions can affect lipids.

Triglycerides

Some guidelines see triglycerides (TG) as an independent risk factor for heart disease. Others state that the evidence for treating moderate triglycerides is less strong.

In the D:A:D study, most of the impact of high triglycerides was explained by other risk factors, but this still remained at +10% per year.

Although there is a lot of individual variability, target fasted levels of under 2.2 mmol/L are considered normal and of 2.2–4.4 mmol/L are borderline. Above this, the risk of heart disease increases.

Levels above 10 mmol/L are very high and need urgent treatment due to the increased the risk of pancreatitis.

Although less that 1.7 mmol/L is a target, treatment would not usually be used unless levels are over 2.3 mmol/L.

Treatment and management

Options to improve lipids include lifestyle changes (diet etc), switching HIV meds and using lipid lowering drugs.

Cholesterol and triglyceride levels can often be improved by diet changes (especially reducing saturated fat, trans fat, cholesterol and alcohol and increasing fibre) and by starting or increasing exercise.

Weight loss, if you are overweight, will have a positive impact on lipids too.

Omega-3 can reduce triglyceride levels. Taking a supplement may be more effective that just changing diet.

For example, a 4 gram (g) daily dose Omacor, (90% omega-3 acid ethyl esters) is equivalent to 150 g mackerel or 700 g tuna or 1.1 kg cod or 280 g salmon or 1.7 kg eel or 850 g shrimps.

Table 7: Lifestyle interventions to improve lipids

Aim	Interventions
Reduce TC and LDL	Reduce dietary saturated fat, trans fat, cholesterol; Increase fibre. Minor impact from exercise/weight loss.
Reduce TG	Reduce overweight, alcohol, dietary fructose and high GI carbs. Eat high fibre and low GI carbs; increase physical activity. Omega-3 supplements.
Increase HDL	Replace dietary trans fat with unsaturated fat; increase activity; reduce excess weight. Only moderate alcohol.

See pages 92 –100 for more information about diet and exercise.

Lipids generally improve after switching away from HIV drugs that cause this.

If diet, supplements, exercise and switching treatment (if appropriate) are not enough, then lipid-lowering drugs are generally more effective. They are widely used and have a low risk of side effects. Fibrates reduce triglycerides and increase HDL cholesterol and statins reduce LDL cholesterol.

Lipid-lowering drugs need to be prescribed by an HIV-specialist as they can interact with HIV drugs. For example some statins should never be used and some require increased or decreased dosing when used with PIs or NNRTIs.

Studies are also looking at metformin (an insulin sensitising drug), rosiglitazone and growth hormone.

A study of HIV positive men looking at the effects of exercise and testosterone found that testosterone significantly reduced levels of 'good' cholesterol (HDL). This is a concern for people with lipodystrophy who already have elevated triglycerides and 'bad' cholesterol (LDL).

Although muscle gain and fat loss were greater in the testosterone group, levels of good cholesterol increased in people who used exercise without testosterone, and this may be more appropriate for people with lipodystrophy.

Although anabolic steroids can increase muscle mass they can also reduce fat, and have the potential to worsen lipoatrophy and lipid levels.

For further information see:

EACS metabolic guidelines (2011)

/www.europeanaidsclinicalsociety.org

ESC/EAS Guidelines for the management of dyslipidaemias (Eur Heart Jour, 2011)

http://eurheartj.oxfordjournals.org

Increased blood-sugar levels and risk of type-2 diabetes

Associated drugs: some protease inhibitors and some nukes.

Glucose and insulin

Glucose is a type of sugar. Your body relies on glucose to provide energy. A hormone called insulin processes the sugar and allows it to enter cells.

Insulin also regulates production of new glucose by the liver, levels of glucose in the blood, and metabolic aspects of fat cells.

Insulin resistance is the term for when this system fails to work properly. Although your body produces more insulin to compensate, if insulin resistance continues, and sugar levels remain high, you can develop diabetes.

Insulin levels are difficult to measure, but glucose levels, usually checked by fasting or non-fasting blood tests, are routinely used for monitoring risk.

Types of diabetes

Type-2 diabetes mellitus (T2DM) is an adult illness that usually develops slowly. It can take years or decades for mild insulin resistance to progress to diabetes, but the impact on the risk of heart disease is serious. Some protease inhibitors increase glucose levels and the risk of diabetes.

Type-2 diabetes is different from Type-1, which is caused by low insulin production, and managed by insulin injections.

Risk of long-term health problems

High untreated blood-sugar is related to many long-term health problems. This can include the kidneys, nerves, eyes and vision, risk of heart disease and stroke, erectile dysfunction in men and pregnancy complications in women.

Diabetes can increase the risk of having a heart attack as much as smoking.

Fat and sugar metabolism are also closely linked and insulin resistance is a complication of HIV therapy that is getting more focus. It is directly related to some protease inhibitors and possibly indirectly related to older nukes through their effect on fat distribution. Changes in blood glucose levels and insulin sensitivity are closely related to other symptoms of lipodystrophy.

What can help

As with HIV negative people, mild insulin resistance can be managed by diet, exercise and stopping smoking. Switching HIV drugs associated with increases in blood-glucose is recommended when appropriate.

Dietary advice involves reducing processed sugars, refined and fast foods, white flour and potatoes as they all cause quick sugar ‘highs’. Complex carbohydrates (wholemeal bread, wholemeal and al-dente pasta, porridge, most vegetables) provide energy more slowly with less impact on sugar levels.

Metformin may help people with insulin resistance and fat accumulation. Pioglitazone may help people with insulin resistance and fat loss. Drug interactions with HIV drugs (PIs and NNRTIs) means that drug-level monitoring (TDM) should be used to confirm dosing.

Tests to diagnose and monitor glucose and insulin levels

Fasting glucose test - measures blood sugar after an 8-hour fast. This should be measured before starting and after switching treatment, and at least annually after this.

Fasting levels over 5.6 mmol/L in plasma indicate insulin resistance, and the need for an oral glucose tolerance test (OGTT).

Random glucose test - Unfasted glucose levels are less accurate but are taken shortly after someone has had something to eat or drink. If it is greater than 5.17 mmol/L other tests are run. Diabetes is over 11.1 mmol/L.

Oral glucose tolerance test (OGTT) - Monitors levels of glucose every 30-60 minutes for two hours after fasting for 8-hours and then drinking a measured glucose drink. Healthy glucose on this test should be less than 3.62 mmol/L. If it is greater than 5.17 mmol/L other tests are run. Diabetes is over 11.1 mmol/L.

Haemoglobin A1c - tests how much glucose adheres to red blood cells. It is used to determine average glucose levels over several months. Without diabetes a normal range is 4-6% and managed treatment for someone with diabetes should aim to keep this under 7%.

Fasting insulin test - and results used to calculate HOMA-IR score (Homeostatic: Model Assessment-Insulin Resistance). Measuring glucose is generally preferred to measuring insulin directly.

Insulin tolerance test (also called glycemic clamp) - where insulin is infused by intravenous line, and glucose given until normal blood sugar levels are reached. This is expensive and again is rarely used.

Symptoms of high blood-sugar, and diabetes

- Feeling thirsty or excessively hungry
- Feeling tired
- Low concentration
- Blurred vision
- Unexplained weight loss
- Frequent need to urinate
- Slow healing of cuts
- Tingling in hands or feet (neuropathy)
- Nausea and vomiting

Risk factors for abnormal glucose

- Liver damage or coinfection with hepatitis C
- Family history of diabetes
- Overweight (BMI >30)
- Lipodystrophy or lipoatrophy
- Low exercise
- Over 40 years old
- High blood pressure (over 130/85 but this depends on age and other risk factors for heart disease)
- High cholesterol and triglycerides (over 1.7 mmol/L) and low HDL (good) cholesterol (less than 0.9 mmol/L)
- History of insulin resistance or high glucose
- Other meds, including niacin, glucocorticoids, megestrol and Growth Hormone and some PIs

For further information see:

EACS metabolic guidelines

www.europeanaidsclinicalsociety.org/

Section 4:

HIV, ageing and quality of life

HIV and ageing

The benefits of ageing

Ageing can bring new positive perspectives to life that are only possible because of our previous experiences.

This can often bring greater personal confidence and assurance. It can include a greater appreciation for time and for making every day count. Sometimes this can bring a freedom from many of the insecurities and uncertainties that are common when we are younger.

Life can still be dynamic and exciting as we grow older. Of course there will be differences compared to when we were younger but these are not bad things.

By looking after our health, staying physically and mentally active and looking forward to the future optimistically, this should be an enjoyable and rewarding time of life.

As ageing involves a higher risk of some health problems, researchers are now looking at how HIV affects ageing.

Many people living with HIV are now in their 50s and 60s and thinking about long-term issues that they never expected. Treatment has been so successful at keeping most of us alive, that life-expectancy is now similar to that of someone who is HIV negative.

While this is true, HIV positive people still have higher rates of many common health complications.

There are also increasing rates of new infections in older people: over 10% of new infections are in people over 50.

Complications of ageing

Ageing brings health issues that can also be important to mention in this guide.

This is because many of the ageing processes involve body systems that are affected by HIV and sometimes by side effects.

These include:

- Physical health: agility, strength, balance and frailty.
- Mental health: neurological problems including memory, concentration, depression and dementia.
- Sensory functions: eyesight, hearing.
- Sexual health and hormone changes.
- Cardiovascular health.
- Lipid metabolism.
- Liver and kidney function.
- Bone health and lower bone density.
- Cancers.
- Social life, isolation and financial security.

Access to healthcare

Medical care of many of these health problems may involve your GP and other health care professionals.

In the UK, some HIV services are routinely being moved to GP care. GPs may have more experience in these areas than your HIV doctor, including:

- Lipid management (although interactions with HIV meds often requires specialist advice).
- Services to help stop smoking.
- Diabetes management.
- Some cancer screening programmes.

Complications that are not managed by your HIV clinic may involve services that have less experience with HIV.

This is an aspect of life that will become increasingly important as routine HIV care becomes normalised.

On the other hand, it will remain just as essential for your HIV doctor to be involved in any HIV-related complications.

Lifestyle choices

Ageing takes planning, so you can take an active role in reducing your risk of many common health complications.

- This includes staying physically active, eating a healthy diet, not smoking, moderate use of alcohol, and keeping mentally active.
- As we get older, our goals are likely to change. Exercise that is less physically stressful can be more fulfilling, as can socialising in bars that are less crowded and noisy. These are all important qualities of life.
- New interests can become more important and have a different quality compared to some of things you did when you were younger.
- Find something to make each day important and have goals for the short, medium and long-term.

Exercise

Daily life can easily become more sedentary and less active: spending more hours on a computer or watching TV.

Unless we stay active, our strength, agility and endurance will reduce. Ageing is associated with poorer physical health. Find time to keep active.

- Walking is the easiest exercise. We get time to breathe deeply, think about our life, see our surroundings and enjoy the seasons.
- Most gyms usually include free initial training and a wide range of classes: yoga, dance, swimming, boxing.
- It is important to talk to your doctor before starting a new exercise programme.

See pages 99–100 for more information about exercise.

Diet: food, drink, cigarettes

What you eat and drink can have a big impact on your health.

- A balanced diet includes vegetables, fruit, proteins, fats and carbohydrates. Eating more fresh fruit and vegetables and less saturated fats and fried food is good for your health.
- High dietary salt increases the risk of high blood pressure, kidney damage and diabetes.
- Alcohol in moderation may have health benefits. Weekly guidelines are up to 21 units for men and up to 14 for women. One unit is a small glass of wine, a half pint of beer or a single spirit measure.
- Cigarettes damage your lungs, blood vessels, cholesterol levels and are associated with an increased risk of numerous cancers.

See pages 92–98 for more information about diet and health.

Heart disease

CVD=Cardiovascular disease

When lipodystrophy and metabolic changes associated with combination therapy became more widely recognised, there was an initial concern that these symptoms could increase the risk for heart attack or stroke.

This is because increased levels of blood lipids can lead to blocking blood vessels (atherosclerosis) and are a well-established risk factor for heart disease.

This concern was prompted by a series of case reports of heart attacks in HIV positive men who were too young to be considered as traditionally at high risk.

However, the risk of heart disease may be increased more by untreated HIV than by HIV meds.

Several large studies have reported results that calm some of these initial fears.

- Benefits of combination therapy still far outweigh the possible slight increased risk of heart disease for most HIV positive people.
- The SMART study found that using HIV treatment with an undetectable viral load was protective of heart disease compared to not being on treatment or having a detectable viral load.
- The D:A:D study reported a small additional increase in risk of heart disease from each year on some HIV meds including lopinavir/r (Kaletra), abacavir and ddI.
- People at high risk for heart disease may need to take any additional risk more seriously.
- Risk factors for heart disease in HIV positive people are the same as for people who are HIV negative.
- Making lifestyle changes that minimise risk factors are now strongly recommended as part of a long term plan for managing HIV positive patients.

There is a lot of information and research about risk factors for heart disease in HIV negative people. This has often come from very large studies (Framingham, Caerphilly etc) that followed a large group of people for many decades. These studies led to the development of risk calculators that are easy to access online (see page 71 for links).

If you put in your age, gender, cholesterol and triglyceride levels and other risk factors such as smoking, you get your 5-year or 10-year risk of heart disease.

People with high risk factors for heart disease who need HIV treatment, should use HIV drugs that are least likely to increase the risk of cardiovascular disease any further. Support for lifestyle changes should also be provided.

Risk factors for heart disease

The following factors increase the risk of heart disease; some of which are fixed and some are modifiable by lifestyle.

Fixed risk factors

- Older age (men over 45, women over 55)
- Gender (men are at higher risk at the same age)
- Family history of heart disease

Modifiable risk factors

- Smoking
- High lipids - ie high cholesterol and/or triglyceride levels
- Lack of exercise
- High blood pressure, especially diastolic blood pressure
- High levels of sugar in blood, insulin resistance and diabetes

Symptoms of heart attack or stroke

Symptoms of cardiovascular disease include:

- Shortness of breath
- Fatigue
- Feeling dizzy or light-headed
- Fainting
- Chest pains (that can extend to the shoulders, back, arms, head and jaw)
- Chest pains after exercise or exertion.

Additional symptoms for a stroke include:

- Sudden numbness
- Paralysis of the face or limbs, especially affecting just one side of the body
- Difficulty speaking
- Loss of balance or coordination
- Severe headache
- Brief loss of consciousness.

If you experience these symptoms, you should seek urgent medical attention.

Rapid treatment after a stroke (within 2-3 hours) can limit permanent brain damage.

D:A:D Study

The D:A:D study is the largest study to look at the risk of heart disease in relation to HIV treatment.

It has been running for over ten years and has collected results from almost 50,000 patients from Europe, the US and Israel.

This diversity is one of the study's strengths. D:A:D found that some HIV drugs are related to a small but significant increased risk of heart disease. This was found in different countries and in both men and women.

These drugs include recent use of abacavir, ddI and cumulative use (from each year) of abacavir, indinavir and lopinavir/r (Kaletra).

Relative rate and actual risk

The D:A:D study showed that the relative rate for an increased risk of heart disease form using a drug depends on your other risks factors.

If you have a low cardiovascular risk, then a relative increase, even by 50% still remains a low real (absolute) risk. However, for someone with a high cardiovascular risk relating to other factors (age, smoking etc) then an increase in the relative risk from an HIV drug would be much more significant.

For someone who has a high risk because of factors that can't be changed (ie a family history of heart disease) then it is more important not to add to these risks by using any HIV drug with this potential side effect.

How to make lifestyle changes

Changing the risk factors for heart disease can have a direct impact on future risk. By implication, this will also make HIV drugs safer to use.

The advice given to the general population is even more important if you are using HIV treatment.

- Stopping smoking is the most important lifestyle change in terms of general health and risk of heart disease. Support groups and other interventions including replacement therapy like nicotine patches are now available on the NHS.

  The most recent research suggests trying a range of products over the first week or two to cope with nicotine withdrawal such as patches, gum, inhalers and sprays so that you find the ones that work best for you.

  Your HIV doctor can refer you to specialist services to help you quit.
- Diet changes can significantly reduce your risk for heart disease.
- Reducing fatty foods can reduce lipids to some extent. Cutting down on salt reduces blood pressure. Eating less processed sugars reduces your risk of developing insulin resistance and diabetes.
- Eat more fruit and vegetables, fish and lean meat and reduce use of processed foods.
- Exercise is the other main factor that you can change. Regular exercise and being more active in your day-to-day life, by walking more and using the lift less, is more important than very vigorous exercise.

  Any change in level of activity will probably have to start gradually. People who start an exercise programme report benefits in quality of life. This can include increased well-being and energy levels.

The website for the North Central London Cardiac Network includes detailed guidelines for managing heart disease:

http://www.nclcn.org.uk/

Glossary (heart disease)

Arteries are the blood vessels that take blood away from the heart.

Veins are blood vessels that delivery blood back to the heart.

Arrhythmia is the medical terms for a disturbance of the heart's natural rhythm. It is called **Tachycardia** when the heart beats too fast and **Bradycardia** when it beats too slowly.

Atherosclerosis refers to a narrowing or hardening of large and medium sized arteries. The narrowing is caused by a build-up of plaque, and usually takes many years. As the walls of the artery thicken, the heart has to work harder to pump the same amount of blood through a narrower gap.

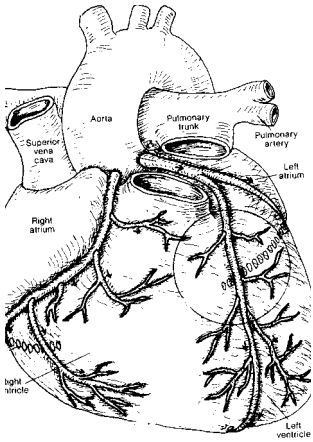
Cardiovascular refers to the heart and blood vessels.

Cardiovascular disease (CVD) is the general term for disease to the heart and related blood vessels.

Cerebrovascular refers to the blood vessels taking blood to the brain. A blockage that restricts blood to the brain is called a stroke. Strokes can occur when blood vessels in the brain block, or when a clot formed in another part of the body is carried to the brain.

Coronary Heart Disease (CHD) refers to the three main arteries that supply blood from the heart. A coronary by-pass is an operation to provide a new route for blood to reach the heart when coronary arteries become blocked.

Hypertension is the medical name for **high** blood pressure (BP). Blood pressure is measured as two numbers ie 120/80.



The first number is systolic BP - the pressure when your heart beats. The second number is diastolic BP, which is the pressure when your heart rests between beats.

Target range for BP is usually quoted as 120/80, with interventions sometimes recommended if this is above 130/85 or 140/90, but these are dependent on risk factors for heart disease including your age.

Hypertension increases the risk of a heart attack, particularly when diastolic BP is high.

Hypotension is the medical name for **low** blood pressure.

Pulmonary hypertension refers to high blood pressure in the arteries taking blood from the heart to the lungs. HIV positive people are more likely to develop pulmonary hypertension than HIV negative people.

Myocardial Infarction (MI) is the medical term for 'heart attack'

Peripheral arterial disease refers to atherosclerosis in the arteries in the arms or legs.

Bone health

(osteo = bone; necrosis = death; porosis= thin)

HIV is one of several conditions that are linked to bone changes.

Even if this is not a side effect of HIV meds this is a new area of research that is important for your long-term health.

There are two main types of bone problems.

- Changes in content and structure of bone. This is where your bone becomes thinner and more brittle. This is called osteopenia at mild levels (when there are no symptoms) and osteoporosis at more severe levels (that require treatment).
- Interruption of blood supply to the bone. This causes death of bone tissue - called osteonecrosis and avascular necrosis (AVN).

Osteopenia and osteoporosis

Rates of both osteopenia and osteoporosis are significantly higher in HIV positive people compared to HIV negative of the same age and sex.

It is still unclear if this is due to HIV or side effects or both.

Although tenofovir can cause a small drop in bone mineral density in the first six months of use, this does not appear to progress with longer use.

The SMART study reported slightly lower bone density in people who were on any treatment, irrespective of which drugs they used.

Bone density reduces with age and a DEXA scan for all post-menopausal women and for men older than 50 is recommended in some HIV guidelines.

Risk factors for low bone mineral density include:

- Age (bone reduces in later life).
- Low body weight and low Body Mass Index (BMI) as heavier people have stronger bones.
- Lipodystrophy and metabolic changes (the way your body processes sugar and fat are linked to bone changes).
- Use of corticosteroids (prednisone).
- Alcohol use (more than 3 units/day).
- Caucasian/Asian race.
- Smoking cigarettes.
- Low calcium or vitamin D levels.
- Lack of physical activity.
- Family history of osteoporosis.
- Low testosterone levels in men and early menopause in women.

Osteoporosis is more serious than osteopenia because it is linked to an increased risk of fractures and pain (commonly to the spine in men and the hip in women).

Diagnosis: DEXA results

A DEXA scan is usually used to diagnose low bone mineral density.

Results are usually given as a T-score which compares your results to a reference group (age 30) matched for your sex and race.

	T-score
Normal	higher than –1.0
Osteopenia	–1.0 to –2.5
Osteoporosis	less than –2.5

If you have osteoporosis you will need advice on how to exercise safely.

Osteonecrosis and AVN

Osteonecrosis and AVN are much less common, and usually affects the hip, shoulder or knee joints, and requires replacement surgery.

It is very common for corticosteroid use to be a contributing factor in cases of AVN.

Early diagnosis of AVN makes a big difference to the success of treatment as well as your quality of life. If you have pain in these joints, ask to see a specialist. An MRI scan is used to make an appropriate diagnosis.

Protecting bones: treatment and prevention

Your bones are a living structure, 10% of which naturally die each year to be replaced by new cells. If the bone isn't replaced quickly enough or in sufficient quantities, your bones become thinner and more brittle.

Leading an active life, and including exercise, maintains healthy bone. This includes weight-bearing exercise (walking, jogging, running, steps and dancing) and muscle strengthening exercise. Improvements include better posture, balance and strength and a direct improvement in bone density.

If you have osteoporosis some common exercises, including twisting and stretching may not be recommmended. Take expert advice.

Treatment and prevention measures are similar to HIV negative people - although closer monitoring of HIV positive people is clearly important.

Stopping smoking and reducing alcohol, taking exercise and eating a diet adequate in calcium, protein and vitamin D (and spending some time in the sunshine) protect you against bone mineral loss.

Bone-building nutrients include calcium and vitamin D_3 (cholecalciferol) and any deficiency should be corrected by increasing dietary intake or use of supplements.

Guidelines recommend adult targets using 1200 mg daily for calcium and 800 -1000 IU/day for vitamin D_3 (for people at higher risk). If you have very low levels (<15 nmol/L) then using higher doses (50,000 IU weekly) for the first few months is recommended.

These nutrients can be prescribed by your doctor and sometimes require special monitoring and dosing.

The target for vitamin D is for blood levels of 25(OH)D to be higher than 75 nmol/L.

Although HIV meds may have a small negative impact on bone strength, the other benefits of treatment usually outwieght this small risk.

First-line medications to improve bone mineral density are a family of drugs called bisphosphonates. These include alendronate (Fosamax) and zoledronate (Zometa). These may only be needed for a few years until a treatment response is achieved.

Links

National Osteoporosis Foundation (US)
www.nof.org
National Osteoporsis Society (UK)
www.nos.org.uk/
Bone Research Society
www.brsoc.org.uk

HIV and cancer

There are several reasons to include information about cancer in this guide.

- Some people are only diagnosed with HIV when their CD4 count is already very low or following a diagnosis of cancer. Very late diagnosis often includes an HIV-related cancer as part of the HIV diagnosis.
- The risk of most cancers increases with age. The longer we live–and luckily life expectancy has never been better–the greater the chance we will have to cope with cancer-related illnesses.
- Although rates of the three AIDS defining cancers (KS, NHL & cervical cancer) have fallen with access to HIV treatment, some non-AIDS defining malignancies (NADM) still occur at a higher rate in HIV positive compared to negative people.
- HIV positive people with side effects from cancer treatment may find some of the information in this guide useful.

HIV, treatment and cancer

Cancers that occur in HIV positive people were originally categorised as either AIDS defining on non-AIDS defining.

Combination HIV therapy has been able to reduce the risk of AIDS defining cancers but seems to have little effect on the risk of some non-AIDS defining cancers but not others. The risk of AIDS defining cancers increases at lower CD4 counts. This is one of the reasons behind the recommendation to start ARV treatment earlier.

To makes things complicated, some non-AIDS defining cancers occur at higher rates in people living with HIV and this may be unrelated to CD4 cell count or HAART use. Many of the NADM that occur more frequently in people living with HIV are linked to a virus. These include anal cancer in men and women (linked to HPV), Hodgkin's lymphoma (linked to EBV) and liver cancer (linked to hepatitis B and C). A few cancers also occur more commonly in HIV positive people but are not linked to known viruses (lung cancer and melanoma).

Many cancers both NADM and ADM such as lymphomas have high chances of being cured and it is very important to seek treatment as soon as possible.

Other cancers don't seem to be linked to either HIV or use of ARV treatment and are not more common in people living with HIV than in the general population. These tend to be cancers that are not linked to another virus, including breast, colon and prostate cancers. These cancers are increasing in HIV positive people using HIV treatment, because they are living longer for these age-related complications to occur.

For all cancers, early diagnosis and treatment is one of the most important factors for recovery.

This is a highly specialised aspect of medical care. If you are diagnosed with any cancer, whether formally HIV-related or not, you need to be treated by an expert in HIV-related cancer.

Table 8: Incidence of cancers affecting HIV positive people and impact of ARVs

	Cancer (virus)	AIDS-defining	HIV risk vs HIV neg.	ARV impact	Comments
AIDS-defining cancers reduced by ARVs	KS (HHV-8) Non-Hodgkin's lymphoma/NHL (EBV) CNS (brain) lymphoma (EBV-related) Cervical cancer (HPV)	Yes Yes Yes Yes	Yes. Before ARVs rates were 70,000x (KS), 700x (NHL) and 3-8 times higher (cervical), respectively.	KS, NHL and CNS lymphoma are significantly reduced by ARVs. Rates of cervical cancer reduced in some studies.	KS generally only seen in people diagnosed late. ARVs are first-line KS treatment. Cervical cancer screening should start at a younger age and be more frequent in HIV positive women.
AIDS-defining cancers not reduced by ARVs	Burkitt's lymphoma.	Yes	Higher.	ARVs improve outcome of cancer treatment but may not reduce the incidence.	
Non-AIDS defining but higher risk in HIV positive people.	Anal cancers (HPV). Hodgkins Disease (EBV) Lung cancer Liver cancer (HBV, HCV) Head and neck cancers (HPV) Melanoma	No No No No No No	Yes, but estimates vary by study. Approx 35x (anal), 10 x (HD), 2–5 times higher (lung, liver, head and neck, melanoma).	Incidence is not reduced by ARVs but HAART is essential to increase survival. Rates increasing due to living longer.	Screening for anal cancer in men and women is not currently routine, although recommended by some experts. Stopping smoking reduces lung cancer. All hepatitis coinfected people should be screened for liver cancer (6 monthly US and AFP). Avoid sunburn.
Not related to HIV or defined as AIDS related. Not affected ARVs.	Breast cancer Colon cancer Prostate cancer	No No No	No No No	Rates are not reduced by ARV treatment. Rates are increasing due to living longer.	Screening recommended as part of general population screening.

This table only refers to cancers in general terms. HIV-related cancers that occur at very low rates are not included. KEY: KS: Kaposi's Sarcinoma; HD: Hogdkins Disease; NHL: Non-Hodgkins Lymphoma; EBV: Epstein Barr Virus; HHV-8: Human Herpes Virus-8; HPV: Human Papilloma Virus; CNS: Central Nervous System.

Lifestyle factors and your health

The following few pages focus on lifestyle changes that can affect your health.

This is because these have been highlighted in many research studies in the general population, see Table 9.

As we get older, these risks and the potential to change them are just as important for HIV positive people.

The risk for all the health complications in Table 9 can be reduced by the linked lifestyle change.

Pages 93–100 include more detailed information about diet and exercise.

Table 9: Lifestyle factors linked to serious health problems

Risk factor	Health conditions
Cigarette smoking	Heart disease, stroke, diabetes, numerous cancers (lung, oesophagus, mouth, pharynx, stomach, liver, pancreas, cervix, bladder, kidney, colorectal), leukaemia, chronic obstructive pulmonary disease (COPD), other respiratory diseases, TB.
High blood glucose (sugar)	Heart disease, stroke, diabetes, renal failure, some cancers (colorectal, breast, pancreatic).
High LDL cholesterol	Cardiovascular disease (heart and stroke)
High blood pressure	Heart disease, stroke, hypertension, renal disease.
Obesity (high BMI)	Heart disease and stroke, diabetes, some cancers (colon, kidney, breast, gallbladder).
High trans fats in diet	Heart disease
High saturated fat diet	Heart disease
Low omega-3 in diet	Heart disease
High dietary salt	Heart disease, stroke, hypertension, stomach cancer, renal failure.
Low dietary fruit and vegtables	Heart disease and stroke, some cancers (colorectal, stomach, lung, oesophagus, mouth and throat).
Alcohol use (above recommended levels)	Heart disease and stroke, hypertension, diabetes, some cancers (liver, mouth, throat, breast, oesophagus, colorectal), cirrhosis, pancreatitis, road injuries, suicide, homicide and other injuries, alcohol use disorders.
Low physical activity	Heart disease and stroke, breast and colon cancers, diabetes.

Diet: a balanced diet and your health

A healthy diet helps your physical and mental health.

It can reduce the risk and severity of conditions such as obesity, heart disease, diabetes, hypertension, depression and cancer.

Why a balanced diet?

Sometimes we eat because we enjoy the taste and experience of different foods, and sharing food and meals are important socially.

But other than for pleasure, our bodies need food to get nutrients, vitamins, minerals and energy.

Very few foods are either all good or all bad - so by having an idea of the balance in your diet, it should be easier to enjoy food and be healthy.

There are seven essential nutrients that come from a balanced diet, and a rough percentage of daily calories should come from each nutrient, see Table 10.

Eating a wide range of different foods will give you body the nutrients and micronutrients that it needs.

A healthy diet should include a varied selection of foods. But some types of food are better for us (”5-a-day” for fruit and vegetables) than others (cakes, biscuits etc), see Table 11.

Diet and weight

In general, if we eat fewer calories than our body needs for energy, we will lose weight and if we eat more than we need we put on weight.

But this is not the whole story. We all have an individual balance depending on how our body signals to itself to process food. Some people burn more energy and in different ways, and this explains some of the diversity in how we all look.

This can also change over time through life depending on whether we are still growing and when we get older.

Some foods are processed by our bodies in ways that are more healthy. This tends to be foods that release sugars more slowly and that contain fibre.

Other foods including saturated fats and foods that are high in salt or simple sugars can have a negative impact on health because of how the body processes them.

Calories and lifestyle

The average number of calories you need each day can vary and is influenced by many factors including sex, age, metabolism, physical activity, growth and pregnancy.

Body height, weight and size, genetics, hormone levels and any illness can affect how much energy we need.

Daily guidelines recommend around 2500 calories for men and 2000 calories for women.

Differences within nutrients

There are healthy and less healthy dietary sources of nutrients, especially for carbohydrates (carbs) and fats. These are explained below and in Table 12.

Carbs: simple vs complex

It is recommended that carbohydrates ("carbs") form the basis of most diets. You should aim for half of total energy (calorie) intake to come from carbs. This food group can be separated into simple and complex carbs

Complex carbs such as wholewheat flour and pasta, and brown rice, contain larger chains of sugar molecules. These take longer to digest than procesed grains. This makes you feel full for longer, helping to control your appetite.

Complex carbs provide energy and are key sources of nutrients such as fibre, B vitamins and minerals.

The more refined complex carbs e.g. white flour, pasta and rice are digested more quickly by the body. This makes them a faster source of energy. However, these types of carbs do not offer as many additional nutrients. This is why whole-wheat and brown carbs helps improve the overall quality of your diet.

Simple carbs are the sugars. These can be natural (e.g. fructose found in fruit) or refined (e.g. sucrose or glucose in soft drinks, sweets and biscuits).

Another key carb-related term is the Glycaemic Index (GI). This relates to how quickly the sugar in either complex or simple carbohydrates is released into the blood stream.

Low GI foods release sugar slowly. This gives a prolonged supply of energy to the body. Higher GI foods give shorter bursts of energy.

The GI of a carbohydrate is affected by numerous factors including whether the carb is simple or complex but also how the food is cooked and also what it is eaten with.

Fruit and vegetables are carbohydrate foods. They include a wide range of vitamins and minerals as well as soluble fibre. You should aim for five portions of fruit and vegetables a day.

Fruit juice is counted as one of your 5-a-day, but if you are watching your weight it is better to eat whole fruit which takes longer to digest and keeps you felling full for longer.

Fat: saturated and unsaturated

Dietary fat is important for making healthy cells. It produces hormones and other signalling molecules and is a source of energy and energy storage.

Two categories of dietary fat are saturated and unsaturated. They have the same amount of calories but different effects on your health. We need to aim for a good balance between the different dietary fats to optimise our health and reduce health risks.

Saturated fats are generally solid at room temperature and these are the fats that will have a negative impact on our health. They are the naturally occurring 'bad fats' and are found from butter, hard cheeses, fatty meat/ meat products, cream, lard, suet and some plant oils including coconut oil and palm oil.

Table 10: Essential nutrients for a healthy balanced diet

Nutrient	% of daily calories	Function	Source
Carbs	45–55%	Energy	Grains (refined & unrefined): wheat, maize, corn, millet, oats, rice, flour, pasta, noodles; potatoes; sweet potatoes, yam. Fruit (sugar).
Protein	10–35%	Tissue growth and maintenance	Meat, fish, nuts, eggs, soya, beans and pulses.
Fat	20–35% from fat	Energy, energy storage, hormone production	Nuts, seeds, plant oils, dairy products (milk, cheese).
Fibre	Included in carbs.	Regulates blood sugar levels, bowel function and bowel health.	Peas, beans, vegetables, fruit, oats, whole grains, brown rice, nuts, seeds.
Vitamins & minerals	trace	Metabolism regulation, aiding cell growth, other biochemical functions	Specific to each vitamin/mineral. A range of vegetables, lean meat, nuts and seeds will cover most peoples needs.
Water	0	Maintaining hydration	Drinking water, other beverages. About 20% of water intake comes from food.

Table 11: Eat more, eat less...

	Food types	Comments
Eat more	Raw and cooked vegetables & fruit (“5-a-day”), nuts, seeds, beans & pulses, whole grain cereals/bread, lean white meat (chicken without skin), fish (especially oily)	Linked to many aspects of better health including reducing LDL.
Eat in moderation	Lean cuts of beef, lamb, pork, shellfish, dairy products (low fat), unsaturated fats (olive oil, vegetable oil). Dried fruit, jams. Sucrose, honey, fructose, chocolate.	These foods can all be an important part of your diet.
Eat less and in limited amounts	Saturated fat (butter, margarine, lard, cheese, cream, high fat milk), trans fat, salt (less than 5g daily). Processed meats/fatty cuts of meat (sausages, salami, bacon, ribs etc). Processed meals (high in fat, sugar and salt). Pastries, muffins, pies, cakes, sweets, etc. Alcohol is high is sugar and calories and is only recommended in moderation.	These foods are not good for your health. Some guidelines include specific recommendations.

Unsaturated fats include the polyunsaturated, monounsaturated and Omega 3 fats and will have a positive impact on our health. Monounsaturated and polyunsaturated fats are found in oils such as olive, rapeseed and sunflower.

Omega-3 and omega-6 are known as essential fatty acids (EFA's) because the body can only get these from diet. They are found in oily fish such as sardines, salmon and mackerel.

Trans-fats are a form of unsaturated fat that rarely exists in natural food but are associated with partially hydrogenated vegetable oils. They are often added to processed foods such as cakes and biscuits and so these should be eaten less often and in small amounts.

Trans fats as cooking oils have been banned in some regions because of their impact on cardiovascular health.

Diet and cholesterol

Cholesterol is a compound similar to fat. It is needed by the body to form the outside barrier of cells (membrane). It can be both made by the body and consumed through sources in the diet. Absorption of dietary cholesterol is complicated and other factors such as genetics can affect the overall level of cholesterol circulating in the blood.

High levels of cholesterol in the blood are associated with damaging arteries and heart disease.

Specifically, having high levels of low-density lipoprotein cholesterol (LDL) and low levels of high-density lipoprotein cholesterol (HDL) in the blood increase the risk of heart disease.

Changes in diet can make a difference though. Choosing foods with more unsaturated fats compared to saturated fats can increase levels of HDL and lower levels of LDL in the blood.

Diet and triglycerides

Similar to cholesterol, triglycerides are fat molecules that aid in metabolism and moving other fats around the body.

Like cholesterol, high levels of triglycerides in the blood have been linked to heart disease.

Table 12: Types of fat and their impact on your health

	Food types	Comments
Saturated	Generally solid at room temperature. Animal fat from meat and dairy fat (butter, cheese, cream). Some plant oils including coconut oil and palm oil.	Less healthy. Linked to high LDL and increase heart disease. Diets high in saturated fat are linked to raising levels of LDL; this can be a risk factor for heart disease. Saturated fat should not be excluded from the diet however, just consumed in smaller amounts (7-10% of fat intake). A range of fats is needed for healthy functioning of the body.
Unsaturated	Vegetable oils like olive, sunflower, and rapeseed/canola oil. Nuts, avocados. Omega-3 (from oily fish or supplements) and omega-6.	Improves insulin sensitivity, LDL and TG compared to saturated fats. Replacing saturated fats by unsatruated fats and carbs reduces the risk of heart disease.
Trans fats	Trans fats are included in processed foods. As a processed cooking oil, it was widely used by fast food outlets for frying.	Trans fats increase bad cholesterol, reduce good cholesterol and are bad for your health, especially “partially hydrogenated trans fats”. They are banned in some countries and US states for use as cooking oils.

Dietary fibre: soluble and insoluble

There are two types of dietary fibre. This can be classed as either soluble (which changes how other nutrients are absorbed in the digestive system) or insoluble, (which is not metabolised and which itself absorbs water).

A mixture of both soluble and insoluble fibre is needed for good health.

Soluble fibre regulates blood sugar levels and balances intestinal pH levels.

Insoluble fibre helps with digestion and elimination by speeding up the passage of food in the digestive system.

Dietary fibre typically contains a proportion of the carbohydrate cellulose, which cannot be digested by humans as we lack the enzyme to break it down.

Vitamins and minerals

Vitamins are chemical compounds and minerals are chemical elements that the body needs in small quantities. They are used by the body for a wide range of functions and very low levels (deficiency) are related to some health complications.

Unless you have a low level of a particular mineral or vitamin, there is unlikely to be a benefit from taking a supplement.

Protein

Protein is essential in maintaining the function of all cells in the body and is also a source of energy.

It is made up by complex combinations of 22 amino acids. Ten of these amino acids can only be obtained by diet.

Although protein is an essential part of your diet, this is also only needed in moderation.

What about salt?

High intake salt and high salt containing foods increases the risk of high blood pressure and therefore increased risk of coronary heart disease.

Most salt in the UK diet comes from processed foods such as pastries, convenience and savoury type snack foods. Tinned foods can also be high in salt so if in doubt check the nutritional labelling.

Recommended intake of salt varies depending on your age, health and other factors. UK guidelines recommend no more than 6 grams a day for adults, which is the equivalent to 2.4 g of sodium.

To convert sodium to salt multiply by 2.5. US guidelines are 5 g/day while recognising that actual average intake is often twice this high.

Ways of cooking?

The way that we cook and prepare food is important. Certain cooking methods are also better at retaining the nutrients within food.

Cooking techniques such as roasting and frying can be less healthy if a large amount of fat (oil or butter) is added during the cooking.

However, you can fry and roast using small amounts of healthier fats such as olive and rapeseed oil.

Grilling and steaming are widely considered to be healthier cooking techniques in most cases.

Further information

The online references for this booklet includes links for further information.

Exercise and staying active

Many sections of this booklet refer to exercise as a way to improve your health.

Table 13 describes different types of exercise and provides some examples and Table 14 highlights some of the related health benefits.

For more information talk to your doctor about the type of exercise that could benefit you most. Often this might just being way to make your life more active.

WHO guidelines recommend at least 1–5 hours exercise each week depending on the type of exercise (see box).

If you have not exercised for a while you will need to build up your strength and stamina slowly.

Exercise is individual to your goals. Some people want to build up muscle, some want to loose weight and others just want to get fit. Each goal uses different types of exercise.

WHO adult guidelines (age 18–64).

1. Aim for at least 150 minutes of moderate-intensity aerobic activity or at least 75 minutes of vigorous-intensity aerobic activity each week – or a combination.
2. Increasing this time (ie to 300 and 150 minutes respectively) will lead to better health benefits.
3. Aerobic activity should last for at least 10 minutes duration.
4. Muscle-strengthening activity should involve major muscle groups on at least two days a week.

The recommendations for children and those over 65 are slightly different but still promote the importance and many benefits of physical activity.

Table 13: Main types of exercise and related benefits

	Examples	Comments
Aerobic	Walking, jogging, running, cycling, rowing, step machines, dancing, skipping, swimming.	Any exercise that makes your heart beat faster and your breathing rate increase is aerobic exercise. Over time, with aerobic exercise, your heart muscles will grow stronger. This also increases blood circulation so which helps clear your blood vessels. As you work harder and for longer periods this exercise starts to use the energy stored in body fat.
Resistance	Press-ups, pull-ups, using free weights or machines.	Any exercise where you use increased weights (and/or increased repetitions) to make mucsles work harder is called resistance exercise. This type of exercise will build up and maintain muscle mass.
Weight bearing	Walking, running, jogging etc. Some weight lifting.	Exercise that puts weight on your bones, helps your bones grow and stay strong. This includes some aerobic exercie like running and some resistance exercise like weight lifting.
Flexibility	Stretching, yoga, pilates.	Exercises that improve the range of motion of muscles and joints

Nutrition and exercise

A balanced diet will give the body all of the nutrients that it needs to repair itself after exercise. See page 93–98 on eating a healthy diet.

Tips to stay active

Your own goals are personal to you. This is not competitive to anyone else.

Your pesonal plan will be based on your goals. Some people want to build muscle and others to lose weight. Get advice for the best exercise for your goal.

If you find an exercise that you enjoy you will be more likely to do it regularly.

Look out for classes that offer a range of activities and sports. Getting into a routine will help - after a few weeks or months this will feel normal.

Exercise with friends can be more fun, and help keep you motivated. Or see this as time to focus on yourself.

Being more active throughout the day makes a difference. Taking the stairs instead of a lift or walking to work for example.

Start slow and gradually build up your level of activity, particularly if this is a new change. It is important to stretch and warm up before and after most exercise.

Table 14: impact of exercise on different health conditions

	Link to exercise	Comments
Diabetes (type-2)	Physical activity reduces risk.	A more active lifestyle reduces risks of metabolic indicators for developing type-2 diabetes.
Heart disease	Physical activity improves aerobic fitness.	Improving aerobic fitness reduces risk of heart disease. Aim for 150 mins or more of moderate-intensity activity per week.
Stroke	Physical activity reduces risk.	Highly-active individuals had a 27% reduced risk of stroke.
Cholesterol Triglycerides	Physical activity is associated with lowering levels in the blood.	Improved lipids are associated with reduced risk of cardiovascular disease. Few studies have looked at exercise and LDL/triglycerides directly.
Depression	Exercise can be used as a treatment or preventative.	Reduces risk of developing depression and can boost self-esteem.
Breast & colorectal cancer	Moderate-vigorous physical activity for 30-60 mins daily.	Lowers risk of developing some cancers.
Ageing	Regular physical activity for over 65's.	Lowers rates of all-cause mortality, 30% reduced risk of falls, and better cognitive function.
Bone health	Resistance exercise increases bone density (and strength).	Moderate-vigorous physical activity performed for 3-5 days a week. 30-60 mins per session increases bone mass density.

Non-HIV drugs

As we age, similar to HIV negative people, we are more likely to have other health complications. These often need medications.

Many of the drugs used to treat HIV also have the potential to interact with other commonly used drugs, including lipid lowering drugs (like statins and fibrates) and antacid drugs (like omeprazole).

This is an area where the pharmacist who gives you your HIV drugs will have most expertise.

It also increases any complication if side effects occur from non HIV meds.

Both your GP and your HIV doctor should know about all medications and supplements you use.

If you do not want to tell the local pharmacy or your GP about your HIV medications, check for interactions with your HIV pharmacist, HIV doctor or nurse.

Your HIV pharmacist will be able to check whether drugs prescribed by your GP interact with your HIV meds.

Write a list of all your meds including the doses to make this easier.

The online drug interaction resource produced by Liverpool University lets you select the drugs in your HIV combination and then check for interactions with other medications. You can then print an individual summary chart.

This resource includes a wide range of potential interactions between HIV drugs and other medications including:

- Antibiotics
- Antifungals
- Antacids and gastrointestinal drugs
- Blood pressure drugs
- Cancer drugs
- Diabetes drugs
- Erectile dysfunction drugs
- Heart disease drugs
- Hepatitis C drugs
- Herbs, supplements and vitamins
- Hormone treatment and steroids
- Immune modulating drugs
- Lipid lowering drugs
- Oral contraceptives
- Painkillers
- Recreational drugs
- Smoking cessation drugs
- Weight reduction drugs (eg Orlistat)

Further information

Liverpool University HIV drug interaction website.

http://www.hiv-druginteractions.org/

References

The information in this guide is based on treatment guidelines and over 380 published studies. The references for these studies are on the i-Base website.

Whenever possible, we used publications that are recent but that are also accessible free as open access online. Many publications provide free access to full text articles after 1–2 years of the publication date.

Where this was not possible, we include a web link to the study summary.

Each of these papers, expecially treatment guidelines, include their own extensive references for more detailed research. These are a good pointer for further information.

Credits

i-Base would like to thank the wide group of HIV positive people, activists and medical professionals who have reviewed the guide, especially Dr David Asboe, Professor Mark Bower, Dr Angelica Kavouni, Dr Mark Nelson, Dr Chlöe Orkin, Karen Percy and Dr Mike Youle.

We would also like to thank the people who contributed the quotations used throughout the guide. Details of the review group are available online.

This guide was written and compiled by Simon Collins for HIV i-Base.

Thanks to Rebecca McDowall for proof comments and to Muirgen Stack for help with the sections on diet and exercise.

Thanks to The Monument Trust for their continued funding support and to No Days Off for the cover design and layout template.

Further information

The BMA guide is a general reference book (not just HIV-related) including illustrated information on how drugs work and on many individual drugs:

'BMA New Guide to Medicines and Drugs'. Produced by the British Medical Association, 2007 7th edition. Published by Dorling Kindersley for £16.99.

Much of the most easily readable and up-to-date information on side effects and HIV is available on the internet.

The following links were correct when we went to press. If you have trouble finding an article or link call the i-Base phoneline on 0800 800 6013 and we'll try to help.

If you are not reading this in electronic format the i-Base website contains all these references as active links - to save you retyping addresses:

http://www.i-base.info/guides/side

Treatment guidelines

Treatment guidelines have good information on managing side effects:

http://www.bhiva.org (UK)

http://www.europeanaidsclinicalsociety.org/ (Europe)

http://www.AIDSinfo.nih.org (US)

Community resources

The Canadian community organisation CATIE has a comprehensive guide to side effects that may cover other areas and options

http://www.catie.ca/sideeffects_e.nsf

AEGiS.org includes an excellent and comprehensive online database of conference abstracts.

http://www.aegis.org/conferences

Many conferences publish studies on the internet and some also let you hear lectures and see slides from some sessions. Important sites for 2011 meetings include:

Conference on Retroviruses and Opportunistic Infections:

http://www.retroconference.org

International AIDS Society Conferences:

http://www.ias.se

Reports from these and other meetings are usually available shortly after the meetings on the following sites:

http://www.i-Base.info

http://www.aidsmeds.com

http://www.aidsmap.com

http://www.natap.org

http://www.thebody.com

A community site with a range of information on fat loss. As well as facial fat loss this is one of the few sites that includes an overview of fat loss from the buttocks.

http://www.facialwasting.org/

General information

Updated non-technical fact sheets on many side effects are available in English and Spanish on AIDS Infonet:

http://www.aidsinfonet.org/factsheets.php

Aidsmap reports on many aspects of HIV and treatment.

http://www.aidsmap.com

BETA, the quarterly newsletter from San Francisco AIDS Foundation includes articles on side effects.

http://www.sfaf.org/beta

Physicians Research Notebook (PRN)

Detailed and more technical articles on many current aspects of treating and mangaging HIV, including side effects.

http://www.prn.org

Websites on drug interactions

http://www.HIV-druginteractions.org

http://www.HIVpharmacology.com

Online calculators

For risk of heart disease and kidney function:

Different calculators use different data sets to calculate cardiovascular and and kidney function (estimated GFR). None claim to be 100% accurate or validated for HIV. See:

http://www.qrisk.org/

http://www.qintervention.org/

A calculator that includes race may help Black/non-Caucasian people:

http://www.epi.bris.ac.uk/CVDethrisk/CHD_CVD_form.html

The D:A:D study developed a 5-year calculator for use in HIV positive people) calculators is at:

http://www.cphiv.dk/TOOLS.aspx

For BMI, smoking etc:

A range of NHS calculators include BMI (for weight) and financial savings (from stopping smoking):

http://www.nhsdirect.nhs.uk/magazine/interactive

Feedback

Your feedback on this guide helps us develop new resources and improve this resource. All comments are really appreciated. Comments can be posted free to:

FREEPOST RSJY-BALK-HGYT, i-Base, 57 Great Suffolk Street, London SE1 0BB.

Or made directly online at: www.surveymonkey.com/s/7CCWBW2

1. How easy was the information in this guide to understand?

☐ Too easy ☐ Easy ☐ Difficult ☐ Too difficult

2. How much of the information did you already know?

☐ None ☐ A little ☐ Most ☐ All

3. Did the information help you feel more confidence when speaking to your doctor?

☐ Yes, a lot ☐ Yes, a little ☐ Maybe ☐ No

4. Which information did you find most useful?

5. Do you still have questions after reading this guide? Please give examples.

Please include a contact email address if you would like us to contact you about this

6. Any other comments?

Contact details (If you would like a reply): Name _____

Email _____ @ _____

i-base
0808 800 6013

i-Base publications

All i-Base publications are available free

Treatment guides are written in everyday language

HTB is written in more technical medical language

Please photocopy or cut out this form and post to

HIV i-Base

4th Floor, 57 Great Suffolk Street, London, SE1 0BB

or fax to 020 7407 8489

or order online www.i-Base.info

Please send me

Guide to hepatitis C for people living with HIV ☐

Changing treatment: guide to second-line therapy ☐

Pregnancy and womens health ☐

HIV & your quality of life: side effects and other complications ☐

HIV testing and risks of sexual transmission ☐

HIV Treatment Bulletin (HTB) ☐

Name .....

Address .....

.....

Postcode ..... **Tel** .....

Email .....

i-Base would like to thank The Monument Trust for their support in funding this publication

Notes

Call us on
0808 800 6013

i-Base Treatment Information Phoneline

Monday to Wednesday
12 noon to 4pm

i-Base can also answer your questions by email or online

questions@i-Base.org.uk
www.i-Base.info/questions