

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

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Watch out for out-of-date information

Talking to your doctor  
General questions  
Changing treatment  
Further information

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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 to the i-Base guide  
to avoiding and managing side  
effects and other complications...

This booklet will help you:

- 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 a new treatment.

I have changed treatment four times since 1996. This has always been related to 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 change, even when I know that other drugs could be better.

As the benefits from treatment are hopefully going to keep me alive for many years, I want to make sure I am on a combination that is effective, easy to take and tolerable—and that gives me the best quality-of-life.”

# Section 1:

## General information

Introduction

General questions

How to report side effects

Side effects diary

How side effects are graded

Side effects, drug levels and genetics

Changing treatment

Side effects and adherence

You and your doctor

## Introduction

HIV treatment is now more effective and simpler to take than it has ever been. It now involves far fewer side effects.

This is the fifth edition of this guide. One of the most important changes for this version has been to remove at least ten pages relating to side effects of older drugs.

With over 25 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 some 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 also problems of 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](http://www.i-Base.info)

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.

## Changes to this edition

This edition includes the following changes:

- It has been updated to include side effects of the latest drugs.
- Information on side effects of drugs that are now rarely used has been reduced in the print edition. This information is now only in the online version. This includes more detailed information on T-20, lactic acidosis, indinavir, d4T and abacavir hypersensitivity reaction. Please go online or call i-Base if you would like this sent to you by post.
- We have expanded information on long-term complications. These may not be side effects but they are essential in getting your best quality of life. For example, the sections on bone and heart problems.
- We have included a new section on HIV and ageing because this an essential part of living well with HIV.

- The guide includes comprehensive references online. There are hyperlinks to over 250 documents organised by subject. These include:
  - The product information for each drug.
  - UK, European and US treatment and management guidelines.
  - Related studies that focus on safety and tolerability of drugs.

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

## Feedback and comments

We welcome feedback and comments. Please see page 98 or use the online survey:

[surveymonkey.com/s/7CCWBW2](https://surveymonkey.com/s/7CCWBW2)

## General questions

### What are side effects?

Side effects are usually the unwanted things that a medicine does, which can be annoying, difficult and in rare cases, extremely serious.

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

Drugs are licensed 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.

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

### Do all drugs have side effects?

Every drug has side effects. 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.

When more serious side effects are possible, they usually occur more rarely.

### How common are side effects with HIV drugs?

Most HIV drugs are very safe, even when the information about side effects sounds worrying. Many common over-the-counter medicines like aspirin or paracetamol have similar potential side effects (see Table 1).

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

Most people starting HIV treatment report one or more side effects.

Sometimes this is because when you start a treatment you are more sensitive to anything that happens, even though it may not be a side effect.

Some placebo studies (where there is no active drug) also report 90% side effects.

### 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 picked up by 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.

## 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 very 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.

[ema.europa.eu](http://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, 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.

[i-base.info/guides/category/arvs](http://i-base.info/guides/category/arvs)

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### 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.*

How are side effects reported?

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.

Language is very important and often not 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.

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.

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.

## 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.

You may be asked to consider entering 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 and are essential if we want new drugs in the future.

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

## Can I change drugs easily?

If this is your first combination, you should be offered at least two choices. 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 use, you can easily change to alternative drugs until you find one that works and is tolerable.

There are more than 25 HIV medications in the UK, including several that include more than one drug in each pill. While you can't quite mix and match them all, 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 how difficult or easy you will find a drug until you take it. The risk of some side effects may be related to your health when you start treatment.

For example, if you have raised liver enzymes, they may increase even higher if you use nevirapine.

If you start with high cholesterol or triglycerides, they may be more likely to increase if you use some protease inhibitors or efavirenz.

## 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<sup>3</sup>. The cut-off for men is 400 cells/mm<sup>3</sup>.

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 people **underestimate** side effects when they talk to their doctor.

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

Unfortunately, some doctors think that their patients **overestimate** side effects.

- They think their patients exaggerate side effects, and that they are not really as bad as their patients 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. 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](mailto:questions@i-Base.org.uk)  
[www.i-base.info/questions](http://www.i-base.info/questions)



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

## 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 understand your side effects and how they affect you, you need to be able to describe them clearly.

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 effects diary from when you start a new drug. Record everything until you next see your doctor.

A side effects diary is included on page 16. Use a new sheet of paper if you need more space and take this with you to your next appointment.

Describe symptoms giving information about frequency, duration, severity and impact on your life.

### Frequency

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?

### Duration

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?

### Severity

How bad are the symptoms?

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

### 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. Tingling in hands/feet | 9. Stomach pains                 | 17. Vivid dreams               |
| 2. Pain in hands/feet     | 10. Hair loss                    | 18. Feeling anxious            |
| 3. Nausea/vomiting        | 11. Body shape changes           | 19. Eyesight changes           |
| 4. Headache               | 12. Weight gain                  | 20. Mood swings                |
| 5. Feeling tired          | 13. Weight loss                  | 21. Feeling depressed          |
| 6. Dry skin               | 14. Changes in taste or appetite | 22. Injection site reactions   |
| 7. Rash                   | 15. Sexual problems              | 23. Yellow eyes, skin or nails |
| 8. Diarrhoea              | 16. Sleep disturbance            | 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
			1	2	3	4	5
			1	2	3	4	5
			1	2	3	4	5

Other comments and questions to ask your doctor:

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## How side effects are graded in research studies

Most information about the risk of side effects comes from the 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 they are 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 mild to moderately – 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 levels	1.25–2.5 Upper Limit Normal	>2.5–5.0 ULN	5.0–7.5 ULN	> 7.5 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 is Therapeutic Drug Monitoring (TDM) appropriate?

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

- In children;
- In people with pre-existing liver or kidney damage;
- When drug levels may be linked to side effects. If you get yellow eyes with atazanavir TDM can help find an effective lower dose.

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 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 need 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.

TDM is paid for in the UK through programmes subsidised by the manufacturers of most PIs and NNRTIs.

Information on TDM:

[delphicdiagnostics.com](http://delphicdiagnostics.com)

Information on drug interactions:

[HIV-druginteractions.org](http://HIV-druginteractions.org)

[HIVpharmacology.com](http://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. Treatment sometimes takes a while to settle down. So what you think may be side effects may not be related to the drugs at all.

Many symptoms then become easier over the first few days and weeks of treatment.

If your initial symptoms are only mild or moderate, seeing whether they settle down before changing treatment, can be good advice.

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

If you can't tolerate one treatment, then changing to another at any time is usually easy. It will not affect your future options.

- Switching drugs can improve your quality of life and still keep your viral load undetectable.
- Never just stop or interrupt treatment without contacting your doctor first.

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 you remain on the same drugs.
- 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.
- If you have a detectable viral load before switching then have a resistance test 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 the treatment that you switched from was causing those symptoms.

Changing only one or two drugs is only recommended when viral load is undetectable prior to the switch.

### Switching nukes

Most combinations involve two nukes: AZT, d4T, ddI, 3TC, FTC, abacavir, or tenofovir.

In general, people still using 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 between them. 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 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, TMC-125) is a new NNRTI that can be used if you have difficulty with nevirapine or efavirenz, Etravirine does not cause CNS side effects.

Rilpivirine (TMC-278) is a new NNRTI that is expected in 2011. Although it still has CNS side effects, this is only at half the rate compared to efavirenz.

### 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 be used without ritonavir.

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

### 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),
- etravirine (an NNRTI), and
- darunavir/r (a protease inhibitor).

Each of these drugs may have a different role as switch options based on their side effects.

For example, raltegravir does not increase cholesterol or triglycerides.

Many of these drugs could also be used as a switch option for people who are currently having trouble with T-20.

Darunavir uses a lower boosting dose of ritonavir than some other protease inhibitors.

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.
- 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.

People in one study who reported higher numbers of side effects after the first month of treatment were less adherent and had lower viral load reductions three months later.

This study provided a idea of the impact of side effects on everyday life. Ninety-four percent of people reported at least one symptom after 4 weeks, which dropped slightly to 88% after 3 months.

**...94% of people reported at least one symptom after 4 weeks... If you are getting side effects, take them seriously and tell your clinic...**

Feeling more tired and having diarrhoea were the most frequently reported side effects, 40% of which were mild and only 7% were severe.

Most importantly, the severity of these side effects reduced over time.

This study was run a few years ago, and treatments in 2010 are much more tolerable. Nevertheless, the conclusion was clear. 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.



## You and your doctor

Developing a good relationship with your doctor and other healthcare workers is essential for your care.

Nurses and pharmacists are excellent sources of support and advice on all aspects of your treatment including on side effects and adherence.

They are able to make referrals to other professionals including dietitians, psychologists and social workers.

Both you and those involved in your care have certain rights and responsibilities. Below is a list of things you can do, followed by the rights you have as a patient.

Although you always have the right to change your doctor or treatment centre, this is best seen as a last resort.

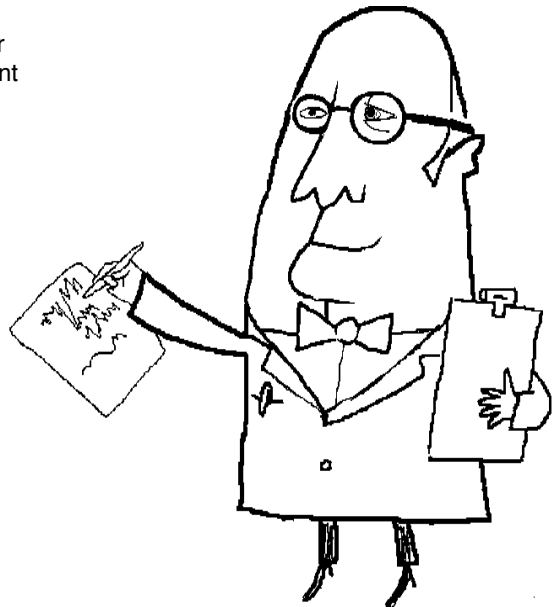
### Things you can do to help...

- Find a clinic that is convenient and that you feel comfortable with.
- Find a doctor who you feel comfortable with: if you're a woman and want to see a female doctor, or a gay man and want to see a gay doctor, then this should be possible.
- Make a list of things you want to discuss with your doctor and take this to your appointment.
- Keep a list of your drugs, dosages, when you need to take them, and whether you get these from your clinic or GP.
- See the same doctor at each visit — this is important. It is very difficult to develop a relationship if you always see a different doctor. However, it is often useful to see a different doctor for a second opinion.
- Plan to have your routine bloods taken 2–3 weeks before your regular appointment. The results will then be available to discuss when you see your doctor.
- Book routine appointments in plenty of time.
- Turn up for your appointments on time. Tell the clinic if you can't make it, so they can give the appointment to another patient.
- Treat all people involved with your care with the same respect you would wish to receive yourself.
- Listen carefully to health advice that you are given and act upon it.
- If you don't understand anything, ask your doctor to explain it again or in a different way.
- Be honest with those caring for you.
- Tell your doctor about other drugs that you take — legal, street, recreational, prescription or complimentary. Alternative treatments and recreational drugs cause side effects and can interact with HIV meds.
- Talk about your adherence (taking your meds). If people managing your care don't know you are having problems, they can't help.
- Be interested in potential research. Studies generate data that can help yours and others future care.



### Some of your rights as a patient...

- To be seen within 30 minutes of your appointment or have an explanation.
- To have options for treatment explained. This includes the risks and benefits of each option.
- To be fully involved in all decisions regarding your treatment and care.
- To be treated with respect and confidentiality.
- For your records to be kept securely and to be available for you to see if you ask.
- To be able to make photocopies of your medical notes.
- To decide not to participate in research without this affecting your current and future care.
- To make a complaint about your treatment without it affecting your future care. To have any complaint fully investigated.
- To receive a second opinion from a suitably qualified doctor
- To receive a written response within 14 days from any letter that you write to your hospital or clinic
- 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 although sometimes this can help resolve a problem if there has been a misunderstanding
- To have all test results and a summary of your treatment history forwarded to your new doctor or treatment centre if you decide to change your clinic





## 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 one of the most common side effects. But it is also one of the least talked about, because it can be embarrassing to discuss.

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

Diarrhoea includes looser and more watery consistency of stool and increased frequency.

It is important that diarrhoea is managed. 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 NRTIs) 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 HIV drugs.

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 will usually clear any 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

- 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 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.
- Drink plenty of fluids to replace the water being lost due to diarrhoea.
- 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 Creon or 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 the maximum dose (8 pills a day for Imodium) and it is still not controlled, ask your doctor for something else.

- Calcium supplements can help reduce diarrhoea associated with nelfinavir and possibly other protease inhibitors. The normal dose is 500mg twice a day and will help those who are avoiding dairy products, which are a major source of calcium in the diet.

- Glutamine has been used experimentally to try and improve bowel function. There is still some debate about the dosage – opinion ranges from 5g to 40g 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
- Calcium supplements
- 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.

### -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.

Fig 1: How opiod anti-diarrhoeals work

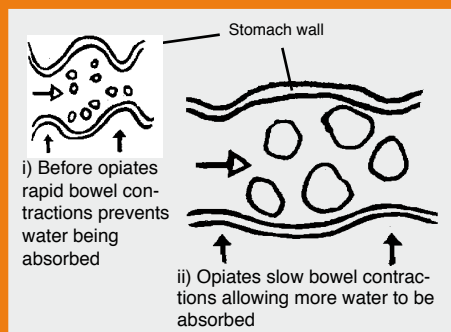
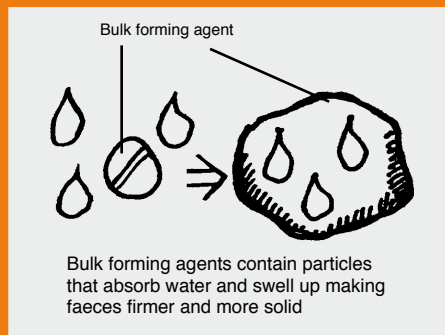


Fig 2: How bulk-forming agents work



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): 10-20mg every 6–8 hours. Suppositories 30-60mg 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 5-10mg, 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: 1.5mg 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. This includes depression, anxiety, sleep problems, other health complications, and social factors like not having work or enough money.

### 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.

## 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.

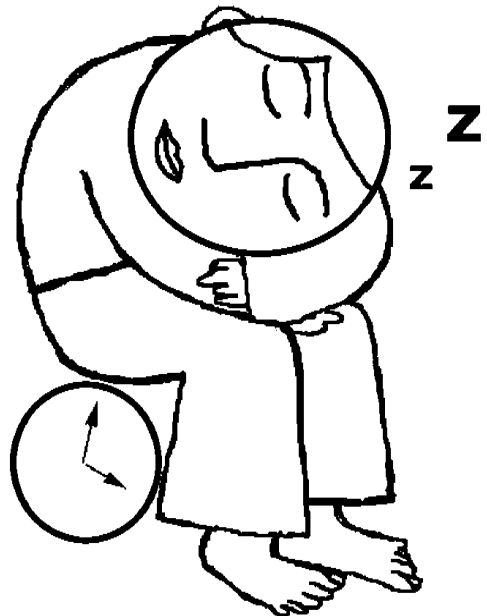
You may be feeling more tired because you are not sleeping properly, and one study found this explained fatigue in over 60% of cases. There is more information about difficulties with sleep on pages 36–37.

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

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 become more 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.

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 manage) 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.

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

HIV-positive people have higher rates of mental health problems compared to similar HIV-negative people.

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 occurring 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 health 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 2010, 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 anti-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 25mg 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

Lactic 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 changes, anxiety, dizziness and disturbed sleep

Associated drugs: efavirenz (Sustiva), Atripla (contains efavirenz), rilpivirine (TMC-278). Other HIV drugs have also been linked to insomnia, though more rarely.

The side effects affecting the central nervous system (CNS) are only associated with efavirenz and rilpivirine (a new NNRTI that is not yet licensed).

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 because 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 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. The advantage of 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:*

- impaired concentration, confusion and abnormal thinking.
- mood swings including anxiety, agitation, depression, paranoia (feeling very anxious or nervous) and euphoria (feeling very happy).
- sleep disturbance 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 women 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, Kivexa

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 screening test are not available for these other drugs.

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 look 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.

## 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 atazanavir 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 bilirubin 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 mg, 150 mg, 200 mg and 300mg. 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-related side effects (renal toxicity)

Associated drugs: Drugs cleared by the kidney with potential for renal toxicity include AZT, 3TC, FTC, tenofovir, Truvada, Atripla, atazanavir and maraviroc. Kidney stones have been commonly reported with indinavir (Crixivan) and rarely with atazanavir and efavirenz.

The kidney is a major organ that:

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

Kidney function can be affected by HIV and other illnesses, including diabetes.

It generally reduces as we get older.

Starting HIV treatment can improve reduced kidney function that is related to HIV. However, several HIV drugs can affect your kidneys and these need to be considered individually.

### Symptoms

Symptoms of reduced kidney function include:

- Needing to urinate more often or less often
- Nausea and/or vomiting
- Feeling tired
- Itchy skin
- Muscle cramps
- Loss of appetite
- Swollen hands or feet or numbness

### Tenofovir-related toxicity

Concerns about kidney-related side effects mainly relate to tenofovir (Viread) and the combinations that include tenofovir (Truvada and Atripla).

This is because tenofovir is now one of the most widely used HIV drugs and because it is mainly processed by the kidneys.

With so many people using tenofovir-based combinations, the research supports this being a safe and well-tolerated drug. Side effects, if they occur, are usually short-term and reversible.

Some studies clearly link tenofovir to an increased risk of kidney-related side effects. These include changes in laboratory test results such as reduced creatinine clearance, low phosphate levels and increased proteinuria (high protein levels in urine). The importance of these changes in markers in the long-term is unknown.

Side effects also include clinical complications including Fanconi's Syndrome that are usually quickly reversible when tenofovir is discontinued.

These risks are likely to be more important for people who already have reduced kidney function.

However, HIV-related kidney disease (including HIVAN) improves after starting combination therapy, even when this includes tenofovir. However, markers of kidney function drop slightly in people who have normal kidney function when they start treatment.

## Tests to monitor kidney function

Routine tests are used to monitor kidney function before and after treatment.

These include:

### Dipstick urine tests

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

### Blood tests to measure protein and creatinine and to estimate glomerular filtration rate (eGFR)

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.

Estimated GFR (measured in mL/min per 1.73 m<sup>2</sup>) is used to grade the severity of kidney damage. Normal levels are higher than 90.

Monitoring should be more frequent for people with mild kidney dysfunction (eGFR 60–90).

With moderate (30–60) or severe (less than 30) kidney function, if there are no alternatives to using tenofovir, guidelines recommend how to reduce the dose.

The risk of kidney toxicity may be higher if you are using other drugs cleared by the kidney, or if you have used these drugs in the past. There is a caution against using other such drugs with tenofovir.

This concern includes using tenofovir and ddI together in combination with a boosted-PI. Until this interaction is

understood, these two drugs are not recommended in the same combination.

Tenofovir is included in the combination pills Truvada (tenofovir+FTC) and Atripla (efavirenz+tenofovir+FTC).

In people who have HIV-related kidney disease, HIV treatment is recommended and is likely to improve kidney function.

Drugs that are metabolised by the kidneys (including AZT, 3TC, FTC tenofovir and maraviroc) include recommendations for using reduced doses in people whose kidney function is reduced (usually indicated by creatinine clearance less than 60 mL/min).

See the individual prescribing information provided with each of these drugs.

## Kidney stones

Indinavir used to be a widely used protease inhibitor, but is now rarely used. The side effect of kidney stones was reduced by drinking an additional 1-2 litres of water daily.

The detailed information relating to kidney stones and indinavir is only available in the online edition of this guide.

In 2007 there were several case reports of kidney stones that contained high levels of atazanavir or efavirenz, showing that this can be a rare side effect with other HIV drugs.

## Skin problems: rash

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

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

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 (Claritin).

**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 caused by an immune-related problem, and from starting nevirapine at a high CD4 count. See pages 62–63 on liver toxicity for more details.

### Other 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)

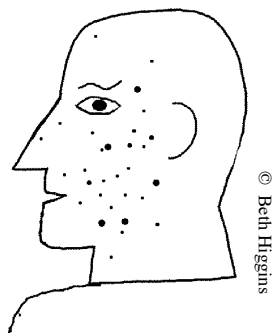
Up to 20% of people using nevirapine, efavirenz or etravirine, can experience a mild to moderate rash in the first weeks of treatment.

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<sup>3</sup> or men if their CD4 count is over 400 cells/mm<sup>3</sup>.

Nevirapine needs to be dosed in two stages. For the first two weeks, you should only take one 200mg tablet, once a day. After the first two weeks the dose increases to two 200mg 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.



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***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 rash requires expert medical assessment.***

### 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 that this has been reported for both head and body hair. Indinavir is rarely used.

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

### Nail and skin 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.

Hydroxyurea and AZT have been associated with nail changes and skin pigment changes in African people.

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 and Atripla.





## 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 a major problem in countries that continue to use d4T (an RTI, or nuke).

PN can be caused by HIV, especially at low CD4 counts (under 100 cells/mm<sup>3</sup>). 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.

### Is neuropathy reversible?

The earlier you switch treatment, and the less severe the side effects when you switch, the more likely that the symptoms will 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. If you have other drugs to use, switching at the first sign of symptoms may be the

## *pain management clinics include a wide range of treatments and expertise*

best thing you can do. Neuropathy can be irreversible and debilitating.

d4T is rarely used in Western countries because of this and other side effects. If d4T is the cause of your neuropathy and you cannot change treatment you can reduce dose. The original twice-daily 40mg dose can be reduced to 30mg or even 20mg twice daily.

After switching, you may have to wait up to two months to know how much this has helped. Often symptoms can continue to 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 1500mg, twice daily, can lead to nerve improvement. Acetyl-L-carnitine can be prescribed on a named-patient basis. Very few clinics in the UK use this treatment routinely.

Research into a synthetic human Nerve Growth Factor (hNGF) in the US which looked promising was then stopped.

### **Painkillers**

Treatments prescribed to manage neuropathy are basically used to mask the pain. Sometimes these painkillers can have side effects themselves which 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) have been used to reduce pain related to neuropathy. They can be prescribed 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.

## Alternative treatments?

Alternative treatments often produce a more acceptable, and more effective, way of managing 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 anecdotally 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** – Topical cream made from chilli peppers that causes increased local blood flow when applied to the skin. Positive reports include a recent HIV-positive study (2010) and approval in Europe to treat diabetic-related neuropathy.

**Volstarol (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).

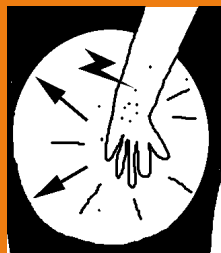
**Vitamin B12** – available as injections, lozenges, or nose-gel. B12 levels should be checked by your doctor. Dosage varies but if levels are too high this can worsen neuropathy.

**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.



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### 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.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 marijuana) 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.

A few HIV drugs have been linked to liver problems. This is why routine blood tests check your liver enzymes (ALT and AST). Liver toxicity becomes a more complicated problem when alcohol use or viral hepatitis have damaged the liver.

Nevirapine is particularly associated with liver toxicity and 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.

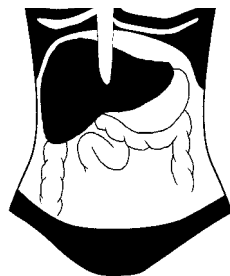
### Nevirapine

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<sup>3</sup> and men should not use nevirapine if their CD4 count is over 400 cells/mm<sup>3</sup>.

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.*

Lactic acid is a by-product formed when the body breaks down starches and sugars. Levels of lactic acid are normally carefully regulated by the liver. Small increases in lactic acid (called hyperlactataemia) are relatively frequent, and are temporary, especially after exercise.

If they reach a higher level, there is a risk of lactic acidosis. This is a potentially fatal side effect related to nucleoside/tide analogues. It is now rarely reported.

Not only are nukes included in nearly all HIV combinations, but the symptoms of lactic acidosis are common side effects or symptoms.

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

Before combination therapy was available, this was only very rarely seen in HIV, and may well have been under diagnosed. Drug packaging now includes a clearer warning about this risk.

Pregnancy may be an additional risk factor for lactic acidosis when using nukes. For this reason d4T or ddI are not recommended during pregnancy when alternative drugs are available.

Lactic acidosis is diagnosed through examination, lab tests and an abdominal CT scan or liver biopsy. Although this toxicity is believed to be a result of damage to part of the cell called mitochondria, there is no simple test for determining people at highest risk.

Although lactic acid in blood can be measured, it is not clear whether high levels increase the risk of lactic acidosis. Over 50% of people showing a high reading on one result, return to normal with the confirmatory test. There appears to be no pattern between high levels and risk of severe toxicity.

Because lactic acid increases with any physical activity, confirmatory tests should be taken after complete rest for at least 20 minutes. Even going to the gym the day before may affect the results.



## 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.

High doses of vitamin B complex with L-carnitine (both IV) until lactate levels normalise improved the chances of survival in one study.

Antioxidants may help to overcome mitochondrial toxicity and use of oral antioxidant supplements such as vitamin C, vitamin B complex, L-carnitine or co-enzyme-Q may help and are prescribed by some doctors.

There are no clear guidelines for restarting nucleoside therapy after a serious case of mitochondrial toxicity. Although caution is warranted, lack of other antiretroviral options has led to people restarting without further toxicity.

Mitochondrial toxicity is thought to be responsible for other side effects including nerve and muscle damage.

### *Diagnosis and treatment:*

- Measure levels of lactic acid and blood pH.
- If lactic levels are over 5 mmol/L and you have symptoms, or if levels are over 10 mmol/L, then stop the HIV medication immediately.
- Use of intravenous anti-oxidants (L-carnitine and vitamin B complex including thiamine, riboflavine, nicotinamide, pyridoxine, dichloroacetic acid and dextranthenol) is recommended.

## 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 is 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 and very high triglycerides (higher than 16 mmol/L). It can also be hereditary (genetic).

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 T-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 2010, very few people are still using T-20. This is because newer drugs, including raltegravir, darunavir and etravirine, 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).

Detailed information on T-20 is included in the online version of this booklet:

<http://i-base.info/guides/side/t-20-injection-site-reactions-isrs-and-other-side-effects>

This includes information on how to minimise ISRs and tips for how to manage other aspects of an injectable treatment.

This information is also available as a separate 6-page PDF leaflet:

<http://i-base.info/qa/faq>

## 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.

Metabolic refers to how the 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 some of these changes (fat loss) is now understood. Hopefully, over the next few years, research will help understand the mechanism behind fat accumulation.

### 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 lipoma - small lumps of fat under the skin).
- 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, exercise and family health.

While most people will not get lipodystrophy, these changes have been reported in men, women and children from a wide range of racial backgrounds.

### How many people are affected?

Depending on what is being defined and measured, “lipodystrophy” has been reported in 5-80% of people on treatment.

It is therefore important to consider each main symptom separately. Lipodystrophy occurs more rarely with current drugs compared to the earliest HIV meds.

The benefits from treatment still clearly outweigh the risks. In the short-term most people do not have serious problems. However, for a minority of people, problems can either become more serious or can occur more quickly.

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

As no one can predict who will be affected before starting treatment, careful monitoring is important. You may try alternative treatments if you get any of these 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 more sensitive to physical changes in their body than their doctors are. 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) is also reliable. (See side bar for more details).
- 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 reduce fat accumulation, have been less helpful, see pages 74–75.

Just because studies haven't shown a benefit, it doesn't mean that other treatments may not be better for you. Whether you decide to change your treatment will depend on several things, including:

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

If you change your combination, you have to change it to one that is 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, using different drugs 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 changes.

**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.

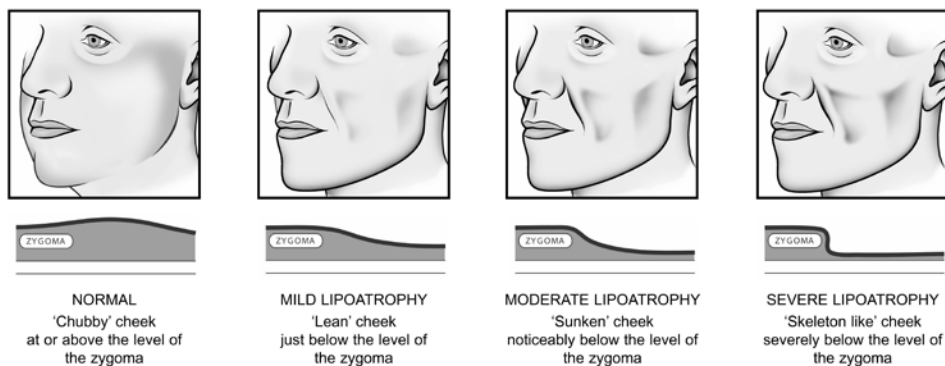
### Switching treatment

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 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 +0.3kg can be detected by scans at 6 months. In one study it took about two years (with an increase of +1.3kg) 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](http://www.facialwasting.org)

However, New-Fill is not equally available throughout the UK. You may have to lobby your 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 injectable 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 has been used to treat more severe facial lipoatrophy because it could be injected in greater volumes. Although the manufacturer claims that BioAlcamid can be removed, it is really a permanent implant. Removal is traumatic and becomes increasingly difficult over time.

Wider use produced increasing reports of serious complications. A Canadian study reported these in 10% of people. These generally relate to infections in the implant, often years after the procedure. This has led to BioAlcamid no longer being used or recommended in the UK.

Anyone who has used BioAlcamid should never have dental injections close to the implant site. They need to inform their dentist about their BioAlcamid implants.

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 that has accumulated as a result of lipodystrophy is not suitable for transplanting.

Although the results were good the process is now less frequently used. This is because it 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 (buffalo hump). It can occur in 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 man's breast is called gynaecomastia.

Abdominal fat accumulation associated with lipodystrophy is generally *visceral* (VAT) rather than *subcutaneous* (SAT) adipose tissue. Visceral fat is around the organs inside the abdomen rather than fat just 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

Many of the approaches used to lower cholesterol and triglycerides are being studied to treat fat accumulation. These include diet, exercise, and investigational drugs.

Using more than one approach may be important. For example, using diet and exercise when switching the drug most likely to be causing problems. And

similarly using diet and exercise when using any treatment.

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 are also likely to worsen fat loss.

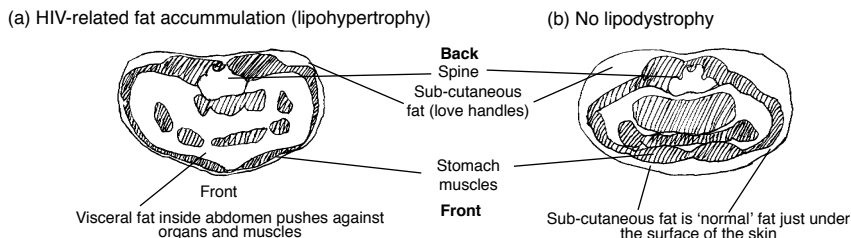
**Metformin** can reduce central fat accumulation in people who already have insulin resistance but should not be used if you have a low BMI.

**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.

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

Tesamorelin only works while to take it and fat return if the treatment is stopped. A 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

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

patient basis. Tesamorelin has not yet been submitted for approval in Europe.

### 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.

Switching from efavirenz can reduce gynaecomastia in men.

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 (lipids) that are carried in blood. These fats perform essential functions, including making effective cell structures and processing vitamins A, D, E and K.

When levels are too high, they increase the risk of heart disease and stroke in HIV-negative people. This is assumed to create a similar risk for HIV-positive people and management guidelines are similar to the general population.

However, if this is a side effect of treatment for a short time, the risk may not be as great as in the general population where abnormal lipids increase and are sustained for many years.

HIV affects lipid levels. Before treatment, cholesterol becomes lower (both good and bad) and triglycerides higher. Starting treatment with any combination will reverse these lipid effects as part of a 'return-to-health'.

Because many HIV drugs also affect lipids this becomes a complex interaction.

### Testing and monitoring

Cholesterol and triglycerides should be checked when you are first diagnosed. They should also be checked 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 you 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.

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

**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 11 mmol/L are considered very high and increase the risk of pancreatitis. EACS guidelines recommend a target of below 1.7 mmol/L.

## Changing HIV drugs in your combination

Lipids generally improve after switching away from HIV drugs that have caused this change.

This usually involves switching from a protease inhibitor (PI) to nevirapine, raltegravir or to another PI that affects lipids less (atazanavir/r or darunavir/r). Tenofovir has a slighter better lipid impact compared to abacavir.

Nevirapine may help by increasing HDL (good cholesterol). The boosting dose of ritonavir to some extent reduces the benefits of protease inhibitors with better lipids profiles.

The debate on the impact of different strategies on reducing risk for heart disease is likely to develop and change over the next few years.

The choice of switch drugs will depend on your previous treatment history and previous history of resistance.



## Diet, exercise and lipid lowering drugs

Cholesterol and triglyceride levels can sometimes be improved or controlled by reducing fat and cholesterol in your diet and by starting or increasing exercise.

Omega-3 supplements can reduce triglyceride levels. This may be much more efficient than trying to obtain sufficient quantities of omega-3 from diet alone.

For example, a 4 g daily dose Omacor, (90% omega-3 acid ethyl esters) is equivalent to 150g mackerel or 700g tuna or 210g herring or 1.1 kg cod or 280g salmon or 1.7kg eel or 850g shrimps.

If diet, supplements, and exercise are not enough, then lipid-lowering drugs (fibrates to reduce triglycerides and/or statins to reduce LDL cholesterol) are recommended.

One study showed that diet changes reduced cholesterol by 4% compared to 17% using a statin.

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 lipodystrophy and lipid levels.

Improved blood lipids have not so far shown an improvement in either fat loss or fat accumulation.

For further information see the European (EACS) metabolic guidelines:

[www.eacs.eu](http://www.eacs.eu)

## 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 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 can increase glucose levels and the risk of Type-2 diabetes.

Type-2 diabetes is different from Type-1, which is usually a childhood illness caused by low insulin production, and which is 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. Normal range for someone without diabetes 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 HepC
- Family history of diabetes
- Overweight (BMI>30)
- Lipodystrophy or lipoatrophy
- Low exercise
- Age over 40
- 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 the European (EACS) metabolic guidelines:

[www.eacs.eu](http://www.eacs.eu)



# Section 4:

## HIV, ageing and quality of life

HIV and ageing

Heart disease

Bone mineral changes

Cancer and HIV

Non-HIV drugs

References

Further information

## HIV and ageing

### The benefits of ageing

Ageing can bring new positive perspectives to life that are only possible because of your 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 you are younger.

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

By looking after your 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 to. 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.

By 2015, more than half of the HIV-positive people in many Western countries will be older than 50 years.

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 reduced bone density
- cancers
- social life, isolation and financial security

### Access to healthcare

Medical management of many of these health complications may also 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 require specialist advice).
- Smoking cessation services.
- 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.

Conversely, 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.

- Just as for HIV-negative people, this includes staying physically active, eating a healthy diet, not smoking, moderate use of alcohol, and keeping mentally active.
- As you get older, your goals are likely to change. Physically you may find less stressful exercises more fulfilling. You may prefer socialising in bars that are less crowded and noisy. These are all important qualities of life.
- New interests will become more important and have a different quality compared to some of things you did when you were younger.
- Finding something to make each day important and having goals for the short, medium and long-term can help.

## Exercise

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

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

- Walking is the easiest exercise. You get time to breathe deeply, think about

your life, and see your surroundings and enjoy the seasons.

- Most gyms usually include free initial training and a wide range of classes: yoga, dance, swimming, boxing.
- *Take medical advice before starting any new exercise programme.*

## 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. Lifestyle changes that can help your health often include eating more fresh fruit and vegetables and eating less saturated fats and fried food.
- Keeping to the recommended amount of salt will reduce the risk of high blood pressure, kidney damage and diabetes.
- Foods high in sugar and salt increase the risk of 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.

There is a direct link between calories in your diet, the energy you use each day and your weight. If you eat more calories than you use you will put on weight and taking less calories will lose weight.

Whatever your goals, these will be easier to achieve and maintain if you plan these as part of longer-term lifestyle changes.

Your hospital dietician can help with details of your own diet.

## 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 HIV than by HIV treatment.

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 protease inhibitor treatment (10%), but not from using NNRTIs. In 2008 D:A:D also reported an increased risk from current or recent use of the nukes abacavir or 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 collected information from over 33,000 patients from Europe, the US and Israel for more than eight years.

This diversity of patients 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 heart disease increased by around 10% for each year of protease inhibitor treatment, after allowing for other factors such as blood lipids. The impact on the use of abacavir almost doubled the absolute risk.

How much this affects your individual risk depends on your other risk factors.

If you have high blood cholesterol for example but no other risk factors, then your absolute risk will still remain low. However, for example, for a 50-year old male smoker who has high cholesterol and is on HIV medication, it is more important to reduce and limit one or more of these factors. This is because each risk factor (like smoking or high blood pressure etc) is added up to get the combined risk score mentioned above.

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 modifiable factor. 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:

[nclcn.org.uk](http://nclcn.org.uk)

## Glossary (heart disease)

**Arteries** are the blood vessels that take blood from the heart to the lungs.

**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.

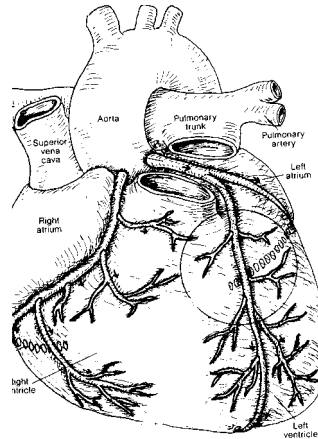
**Cardiovascular** refers to the heart and blood vessels.

**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 mineral changes

(osteonecrosis = bone; necrosis = death; porosis = thin)

HIV is one of several conditions that are linked to bone changes.

Even though this may not be a side effect, we have included information as 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.

In some studies, PI-based combinations have been linked to reduced bone mass. The SMART study also reported slightly lower bone density in people who were on any treatment.

Tenofovir can cause a small drop in bone mineral density in the first six months, but this does not appear to progress with longer use of treatment.

Bone density reduces with age and a DEXA scan for all post-menopausal women and to men over 50 is recommended in some HIV guidelines.

Risk factors for osteopenia and osteoporosis:

- Age (bone reduces in later life).
- Low body weight and low Body Mass Index (BMI); 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.

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.

Exercise that involves twisting and stretching may not be recommended if you have osteoporosis - ask for advice.

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.

Osteopenia is very common in older people and several studies showed high levels in people with lipodystrophy.



Osteoporosis is a more serious progression of osteopenia and can be diagnosed with a DEXA scan. Unlike osteopenia this can lead to fractures and pain (commonly to the spine in men and the hip in women).

### **Osteonecrosis and avascular necrosis**

With osteonecrosis and AVN, inadequate blood supply reaches the bone, and these tissues then die. It is much less common, and usually affects 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 experience pain in these joints, ask your doctor to refer you to a specialist, and to provide an MRI scan so that they can make an appropriate diagnosis.

### **Protecting bones**

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<sub>3</sub> (cholecalciferol) and any deficiency should be corrected by increasing dietary intake or use of supplements.

The National Osteoporosis Foundation 2008 guidelines (U.S.) recommend adult targets using 1200mg daily for calcium and 800 -1000 IU/day for vitamin D<sub>3</sub> (for people at higher risk).



If you have very low levels (<15 nmol/L) then using much higher doses (10–50,000 IU) in the first 1–2 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.

Bone damage may be linked to mitochondria damage and use of HIV drugs from the NRTI family.

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)  
[nof.org](http://nof.org)

National Osteoporosis Society (UK)  
[nos.org.uk](http://nos.org.uk)

Bone Research Society  
[brsoc.org.uk](http://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.
- There are 3 AIDS defining cancers (KS, NHL & cervical cancer) and the rates of these have fallen with access to HIV treatment. Others cancers that are non-AIDS defining malignancies (NADM) seem less affected, and occur at a higher rate in HIV-positive people than in similar HIV-negative populations. These include some traditional HIV-related cancers and others that are not categorised as being HIV-related.
- 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 or 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 make 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 oncology.

**Table 7: 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)	Yes	Yes.	KS, NHL and CNS lymphoma are significantly reduced by ARVs.	KS generally only seen in people diagnosed late. ARVs are first-line KS treatment.
	Non-Hodgkin's lymphoma/NHL (EBV)	Yes	Before ARVs rates were 70,000x (KS), 700x (NHL) and 3-8 times higher (cervical), respectively.	Rates of cervical cancer reduced in some studies.	Cervical cancer screening should start at a younger age and be more frequent in HIV-positive women.
	CNS (brain) lymphoma (EBV-related)	Yes			
	Cervical cancer (HPV)	Yes			
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).	No	Yes, but estimates vary by study.	Incidence is not reduced by ARVs but HAART is essential to increase survival.	Screening for anal cancer in men and women is not currently routine, although recommended by some experts.
	Hodgkins Disease (EBV)	No			
	Lung cancer	No	Approx 35x (anal), 10 x (HD), 2-5 times higher (lung, liver, head and neck, melanoma).	Rates increasing due to living longer.	Stopping smoking reduces lung cancer.
	Liver cancer (HBV, HCV)	No			
	Head and neck cancers (HPV)	No			
	Melanoma	No			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 by HIV treatment.	Breast cancer	No	No	Rates are not reduced by ARV treatment.	Screening recommended as part of general population screening.
	Colon cancer	No	No		
	Prostate cancer	No	No	Rates are increasing due to living longer.	

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.

NOTE: This table only refers to broad cancers in general terms. HIV-related cancers that occur at very low rates are not included.

## 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 pharmacy where you get drugs from 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
- Cancer drugs
- Diabetes drugs
- Erectile dysfunction drugs
- Heart disease and blood pressure 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

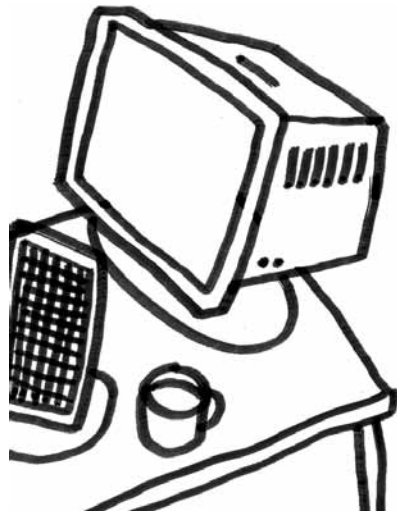
The information in this guide is based on treatment guidelines and over 350 published studies. The references for these studies are on the i-Base website.

[i-base.info/guides/references-side-effects](http://i-base.info/guides/references-side-effects)

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, especially treatment guidelines, include their own extensive references for more detailed research. These are a good pointer for further information.



## 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:

[bhiva.org](http://bhiva.org) (UK)

[eacs.eu](http://eacs.eu) (Europe)

[AIDSinfo.nih.org](http://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

[catie.ca/sideeffects\\_e.nsf](http://catie.ca/sideeffects_e.nsf)

AEGiS.org includes an excellent and comprehensive online database of conference abstracts.

[aegis.org/conferences](http://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:

[retroconference.org](http://retroconference.org)

International AIDS Society Conferences:

[ias.se](http://ias.se)

Reports from these and other meetings are usually available shortly after the meetings on the following sites:

[i-Base.info](http://i-Base.info)

[aidsmeds.com](http://aidsmeds.com)

[aidsmap.com](http://aidsmap.com)

[natap.org](http://natap.org)

[thebody.com](http://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.

[facialwasting.org](http://facialwasting.org)

## General information

Updated non-technical fact sheets on many side effects are available in English and Spanish on the New Mexico AIDS Infonet.

[aidsinfonet.org/factsheets.php](http://aidsinfonet.org/factsheets.php)

Aidsmap reports on many aspects of HIV and treatment.

[aidsmap.com](http://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 managing HIV, including side effects.

<http://www.prn.org>

## Websites on drug interactions

<http://www.HIV-druginteractions.org>

[HIVpharmacology.com](http://HIVpharmacology.com)

## Online calculators

### For risk of heart disease and kidney function

Different calculators use different data sets. None is 100% accurate or validated for HIV.

[cvrisk.mvm.ed.ac.uk/calculator/bnf.htm](http://cvrisk.mvm.ed.ac.uk/calculator/bnf.htm)

A calculator that includes race may help Black/non-Caucasian people.

[epi.bris.ac.uk/CVDethrisk/CHD\\_CVD\\_form.html](http://epi.bris.ac.uk/CVDethrisk/CHD_CVD_form.html)

A research site with heart risk (including a 5-year calculator from the D:A:D study developed for use in HIV-positive people) and kidney function (estimated GFR) calculators.

[cphiv.dk/TOOLS.aspx](http://cphiv.dk/TOOLS.aspx)

### For BMI, smoking etc

A range of NHS calculators include BMI (for weight) and financial savings (from stopping smoking).

[nhsdirect.nhs.uk/magazine/interactive](http://nhsdirect.nhs.uk/magazine/interactive)

## Credits

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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  
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Not-for-profit copying and translations are encouraged or contact the i-Base office for additional free copies.

## Notes

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## Notes

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## 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: [surveymonkey.com/s/7CCWBW2](https://surveymonkey.com/s/7CCWBW2)

1. How easy was the information in this guide to understand?

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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

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- HIV & your Quality of Life: Side Effects and Other Complications ..... ☐
- HIV Treatment Bulletin (HTB) ..... ☐

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