

Guide to hepatitis C for people living with HIV

April 2017

*“modern HCV drugs
(DAAs) cure 95% of
people with simple
treatment ... and
getting these meds is
becoming easier”*

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Written and compiled by Simon Collins and Tracy Swan for HIV i-Base.

Thanks to a review group of people living with HIV and HCV and to the medical advisory group for medical comments.

Not-for-profit copying is encouraged or call for additional free copies.

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.

HIV and HCV information dates quickly, please call to see if an up-date is available.

Thanks to MAC AIDS Fund for funding this guide.

Welcome to the i-Base guide to HIV and hepatitis C coinfection.

This booklet will help you:

- Have accurate, up-to-date information about HIV and hepatitis C coinfection.
- Get the most out of your relationship with your doctor and other health professionals.
- Feel more in control of your health and your treatment options.
- Know about NHS treatment and about the option of buying generic meds online.

“Having had HCV all my adult life and having had previous treatment fail me, I can’t quite believe that I am really now cured.

I have the six-month viral load result in a couple of weeks and I am still wanting to hear it, just to believe it is really true.

It may be psychological but I also think I now have more energy.”

– Robert

Introduction

This is an exciting time for hepatitis C (HCV) treatment because there are so many effective new meds.

Direct-acting antivirals, called DAAs, cure more than 95% of people. Treatment usually takes only 12 weeks and has few side effects.

DAAs are available on the NHS. However, the high price of these drugs means that treatment might involve a wait.

As this booklet went to print, most people with HIV/HCV coinfection are steadily accessing treatment.

When access to treatment is not available quickly some people are buying their own generic treatment at a fraction of the cost to the NHS – although this is not likely to be an option for everyone.

Even if you are waiting for access to DAAs, when you do get these drugs, they are likely to be very effective.

Glossary

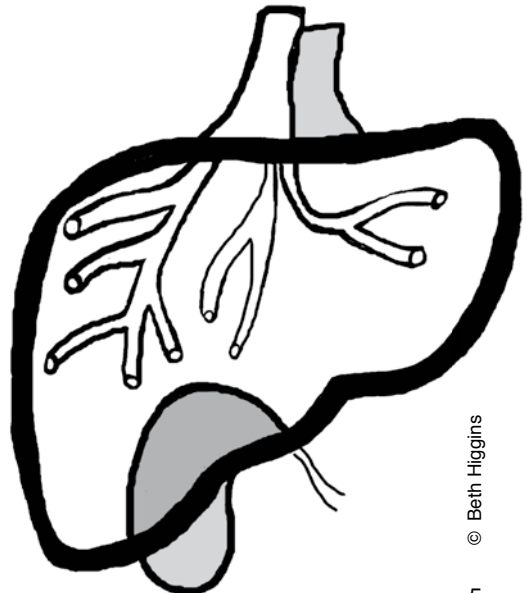
DAAs Direct-acting antivirals (new HCV drugs that directly target the virus)

This guide is therefore a much shorter version compared to previous editions.

New information is included on the range of DAAs, getting access and buying generic versions of HCV drugs online.

In contrast, information about managing HCV without treatment and about interferon and ribavirin treatment is now only available online, together with other information that is less relevant in the DAA age.

Please also check the i-Base website for updates to this guide as new information becomes available.



HCV - but that is now

If you are reading this guide it is likely you have recently been diagnosed with HCV. Or you might have been diagnosed for several years and are now thinking about treatment.

Either way, you might want to know about treatment first. Before any details about transmission, diagnosis, monitoring or even choice of meds.

These first two pages cover news about current treatment. There is then more detail about everything else.

The good news – very easy to report – is that new HCV drugs are so effective that at least 95% of people using treatment will be cured.

- These meds are safe with few side effects.
- Treatment takes only 8 to 24 weeks.
- These are oral drugs, sometimes with just one pill a day.
- Even though they are expensive for the NHS to buy – currently more than £30,000 for a course – people with coinfection in the UK are steadily being treated.
- Many of these drugs are very cheap to manufacture. Generic versions available online are much cheaper – making this an option for some people.

HCV in a DAA world

So in an ideal world, this guide would be a one page leaflet.

You would find out you have HCV, you would be treated quickly, and cured.

- You would not need monitoring to see if HCV is damaging your liver.
- You would not need to know the type of HCV that you have (the next DAAs will treat all subtypes of HCV).
- You would rarely need a liver scan (unless your liver is badly damaged) – even though scans are now easy and painless.

Just test, treat and cure.

And if everyone was treated, your risk of reinfection would also become almost zero. This is because if most people are also cured, the chances to catch HCV again would also be low.

easy to cure?

HCV in the UK

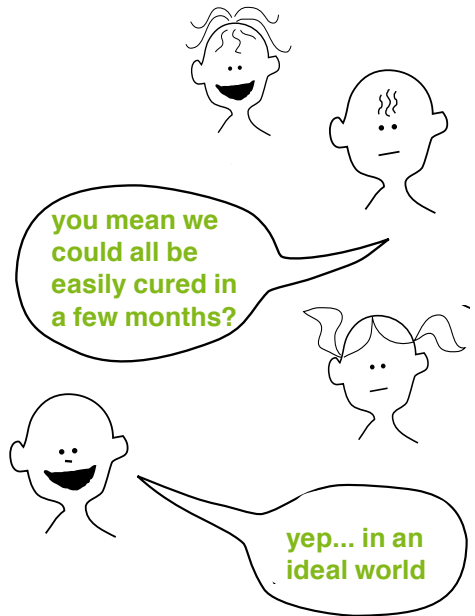
If you do not have access to DAAs, your HCV care will be a bit more complicated. It will involve monitoring, scans and likely delays before treatment.

In the end, you are still likely to be cured, but this process will take time.

How quickly you get DAAs will depend on your individual health – mainly on the degree of liver damage. But it might also depend on where you live and where you are treated.

Another option is to buy generic treatment at much cheaper prices that the NHS has to pay. For more information about UK access, including buying meds online, see pages 41 to 43.

Having to buy treatment might not be fair, when meds should be free, but as it is an option in the UK, we include these details in this guide.



Over time, the prices charged for HCV drugs will become lower and access to treatment will increase. And some countries are already negotiating bulk discounts so that everyone can be treated.

So there are still lots of reasons to be optimistic – just that currently, life might be more complicated... compared to an ideal world.

Coming next...

- HCV transmission – see pages 8 to 17.
- HCV testing and monitoring – see pages 18 to 29.
- HCV treatment – see pages 30 to 43.

HCV and transmission

What is hepatitis C?

Hepatitis C is a liver disease caused by the hepatitis C virus (HCV).

HCV is mainly in blood but it also gets into liver cells where it can cause inflammation and scarring.

This scarring is called fibrosis when it is mild and cirrhosis when it is more serious. Liver scarring reduces how well the liver works.

Usually, it takes many years before HCV causes liver damage, but sometimes this can happen more quickly.

New HCV drugs (DAAs) have the potential to prevent (and sometimes partially reverse) serious fibrosis and cirrhosis – and to cure nearly everyone.

Glossary

ART Antiretroviral treatment (HIV meds).

cirrhosis Severe scarring of the liver that makes it difficult for it to keep working.

fibrosis Mild liver scarring that still lets the liver continue to function.

How HCV is caught and passed on

Most HCV infections come from blood-to-blood contact. This is when blood containing HCV directly enters another person's bloodstream.

Semen and genital fluids and rectal fluid may be infectious but there is less research on this.

Saliva and tears are not infectious.

As with HIV, you cannot transmit or catch HCV by touching, kissing, hugging, or from sharing cutlery, cups or dishes.

Unlike HIV, which dies after a few minutes outside the body, HCV remains infectious for days to weeks, even after blood has dried. This is why you should not share items that might have traces of blood.

Ways that HCV can be transmitted:

- Sharing items that may contain blood, such as razors, toothbrushes, nail scissors and nail files.
- Injecting, smoking or snorting drugs with shared, unsterilised equipment.
- Tattooing or piercing when needles, ink, inkwells and other equipment are shared.
- Medical or dental procedures with unsterilised equipment, including kidney dialysis.
- Needlestick accidents to health workers.
- Sex with someone who has HCV – though this is a complex subject (see pages 10 to 16).
- To a baby during pregnancy, labour or at birth (see page 17).

- From a blood transfusion or blood products (for clotting factors), generally many years ago. Now that blood is screened, this risk is now virtually zero in the UK, Western Europe and the US. Up to 90% of people with haemophilia were infected with both HIV and HCV before 1985.

In some countries, HCV infections still occur from reused, unsterilised equipment during medical or dental procedures or unscreened blood transfusions.

Injecting drug use and HCV

Worldwide, most HCV infections are related to injecting drugs. This includes medical and non-medical settings, from sharing needles and other equipment.

HCV is a tougher and smaller virus than HIV and is less easily killed. It can remain infectious for days to weeks.

Cleaning syringes with bleach reduces the risk of HIV transmission, but it is less effective against HCV. Sharing syringes (even measuring syringes), cotton, water and ties can also be a risk for HCV.

Using clean needles and your own works each time you inject stops both HIV and HCV transmission (and reinfection).

It also reduces the risk of other infections.

Shared equipment for injecting recreational drugs (slamming) including mephedrone and crystal meth in UK gay clubs and/or sex parties has a high risk of HCV transmission (see pages 12 to 16).

People who inject drugs often face barriers to HCV treatment. Page 40 includes information about access to HCV treatment for people who inject drugs.

HCV and non-injecting drug use

HCV is more common among non-injecting drug users than the general population. It is not clear why.

It may be possible to catch HCV from snorting drugs through shared straws or rolled bank notes, or from sharing pipes to smoke crack or methamphetamine.

Sharing these items is therefore not recommended.

Recreational drug use is one of the main risk factors associated with sexual HCV transmission in gay men (see pages 12 to 16). This is because these drugs can affect biological, physical and behavioural risk factors.

Other viral hepatitis infections

Information about other types of viral hepatitis (A, B, D, E and G) is included online.

This includes risks for transmission, vaccines (for hepatitis A and B), treatments and other information.

See page 35 for important information about using DAAs if you have both HBV and HCV coinfection.

HIV, HCV and sexual transmission

Sexual transmission of HIV

The majority of new HIV infections globally each year are from sexual transmission.

The ways that HIV is transmitted are well understood. HIV is present in blood, semen, genital fluids and breast milk.

Different types of sex carry different risks. For example, oral sex is usually low risk, and anal or vaginal sex without a condom is usually high risk, unless the positive person is on treatment or the negative person is using PrEP.

HIV is very difficult to catch if an HIV positive person is on treatment or if the HIV negative person is on PrEP, even without using condoms.

Otherwise, condoms are very effective at stopping HIV transmission, and other sexually transmitted infections (STIs).

Some STIs, including herpes, gonorrhoea and syphilis, can increase the risk of transmitting HIV.

- Genital fluids are more infectious.
- An open sore is an easy route of infection.
- Immune responses to an STI make it easier for HIV to take hold.

All of this information is important when talking about HCV.

Sexual transmission of HCV

The risk for sexually transmitted HCV is more complicated than HIV.

HCV is still primarily a blood borne infection, so sex that includes contact with blood has the highest risk.

Although HCV has been found in semen, rectal and vaginal fluids, it is unclear how infectious these fluids are, because HCV levels are often very low.

However, some studies have reported high HCV levels in semen that are independent of HCV levels in blood.

The risk of HCV sexual transmission is low from vaginal sex, in monogamous, HIV negative heterosexual couples in which one partner has HCV. However, much higher rates of sexual transmission have been reported in HIV positive gay men for reasons that are not clear.

The importance of two aspects of this increased risk still have to be explained.

1. The role of HIV, perhaps because of reduced immune protection or higher HCV viral load in HIV positive people with HCV coinfection.
2. The type of sex some HIV positive men have (behaviour differences) and how this may be different to HIV negative gay men as a group. This may be because of a higher risk of blood-to-blood contact.

Because cases of HCV have been reported where sexual transmission is the most likely route – both from heterosexual and gay sex – UK guidelines currently recommend that people with coinfection use condoms.

“I contracted HCV sexually, and had lived with it for about four years.

Unfortunately, my liver was already in bad shape due to taking antibiotics in my childhood. So HCV progressed quickly over two years.

After trying, in vain, to get DAA access through the health system, I contacted a buyers’ club in South-East Asia and bought the medicine there.

My treatment with generic sofosbuvir and ledipasvir (Safino-L) – which cost US \$1050 – was surprisingly easy.

The indescribable improvement in my quality of life was very revealing. It was only when I was cured that I realised how miserable I had felt before.”

– Tamás

Heterosexual transmission of HCV

The risk of heterosexual sexual transmission of HCV in people who are HIV negative is so low that condoms are not routinely recommended.

The risk is generally reported as less than 1% per year.

In these studies, couples did not use condoms, but also did not have anal sex or have sex during menstruation. So the low transmission rate might be from not having blood-to-blood contact.

Although contact with menstrual blood has not been reported as a common factor in heterosexual partners, this has not been well studied.

In HIV positive people, the risk for sexually acquiring HCV is higher than that reported for monogamous, HIV negative heterosexual couples.

One study reported that sexual exposure is a risk factor for HIV positive women who do not inject drugs but have male partners with HCV.

There is very little information about whether these women were using HIV treatment and whether their HIV viral load was undetectable, or about the HIV status of their partners.

Sexual transmission of HCV among gay men

HCV sexual transmission among HIV positive gay men has been reported in cities in the UK, Europe, Asia, Australia and the US.

In the limited research from these reports, sexual HCV transmission was linked with several risks, which may or may not be directly related:

- Being HIV positive.
- Recreational drug use.
- Group sex and sex parties.
- Sharing sex toys.
- Rougher sex (longer fucking or fisting).
- Barebacking (insertive or receptive anal sex without condoms),
- Other STIs (especially syphilis).
- Meeting partners online.
- Number of partners.
- Rectal bleeding from surgical procedures and/or rough sex.

As many of these experiences overlap, it is difficult to identify the exact cause.

Some HIV positive gay men have caught HCV sexually without these risks, for example, without fisting, using recreational drugs or taking part in group sex.

A summary of safer HCV sex for gay men is included on page 15.

“Finding out I had HCV was like getting an HIV diagnosis all over again. It changed how I thought about sexual risk.

There was no co-infection support group when I first went. I was the only HIV positive man at a support group... but it was tremendously useful. I got just as much from helping other people as I did from their support.

The Hepatitis C Trust also run a fantastic helpline and everyone there either has HCV or has had it in the past. They really understand what support means.”

HIV as a factor

HIV seems to be an important factor in catching HCV because sexual transmission in HIV negative gay men is not as common.

Even with ART, a high CD4 count and low viral load, immune responses to HCV are lower than in HIV negative people.

This is shown by a lower rate of spontaneous HCV clearance and a longer time to develop HCV antibodies.

HIV positive people may also be more infectious, as HCV viral load is higher (by about 10 times) compared to HIV negative men.

The role of blood compared to genital fluid?

When HCV is detected in genital fluids, virus levels are generally low; levels in blood are much higher. Blood is therefore likely to be much more infectious compared to semen during the first six months of HCV infection (called “acute”).

In the few studies measuring HCV in semen, one found higher levels in HIV positive compared to HIV negative men and one found no difference.

This second study found that acute HCV was linked to higher HCV levels in semen than in chronic infection (infection for more than six months).

Although higher HCV viral load increases the chance of HCV in semen, some men have very high HCV in blood and undetectable levels in semen.

HCV is also found in rectal fluid.

Recreational drug use and HCV infection

Although HCV is transmitted during sex among HIV positive gay men, recreational drug use increases this risk in several ways.

This includes non-injection use of crystal meth, cocaine and ecstasy.

Recreational drugs can lower your immune responses so you may be more vulnerable to HCV infection.

Recreational drugs can dilate blood vessels make the lining of the anus more vulnerable to tears and bleeding.

Recreational drugs can act as muscle relaxants allow longer and more energetic sex.

Recreational drugs also reduce inhibitions and are commonly used during group sex.

Injecting recreational drugs, including mephedrone and crystal meth, has a high risk of HCV transmission if needles and other equipment are shared.

Antidote is a drug and alcohol service for lesbian, gay, transgender and bisexual people, based in London with a national phoneline.

020 7833 1674

10am to 6pm, Monday to Friday

<http://londonfriend.org.uk>

Safer HCV sex for gay men

Even though safer sex advice is often similar for both HIV and HCV, the risk for HCV is more likely to be linked to blood than sexual fluids.

- **UK guidelines recommend condoms.**
- Use a new condom with each partner.
- **Use latex gloves for fisting and a new glove with each partner.**
- Condoms and gloves need to be thrown away more carefully than when just considering HIV. Unlike with HIV, the outside of the condom (or glove) may be more infectious than the inside.
- **Any cause of anal bleeding, including recent surgery, increases the chance of HCV sexual transmission.**
- Blood is likely to be more infectious compared to semen or rectal fluid during chronic HCV. Semen might be more infectious during acute HCV.
- **Don't share lube from a pot. Traces of blood will not be visible and HCV remains infectious out of the body for at least 16 hours and perhaps for days or weeks.**
- Recreational drugs can increase the risk of bleeding because blood flow is increased. They can enable sex to be rougher or to go on for longer and they can reduce someone's awareness of their risk.
- **Use condoms on sex toys. If you share sex toys, use a new condom every time.**
- Be aware that in group sex HCV can be transmitted by someone who does not have HCV themselves, for example, from onward contact with traces of blood from a previous partner.
- **Other STIs are linked to acute HCV infection. Routine health checks are easy. Early diagnosis and treatment are important ways to look after your health and your partners health.**

Type of sex, group sex and sex parties

Any activity with a risk for contact with traces of blood (rather than semen, which is the route for most STIs) is likely to be significant for HCV transmission.

Semen may be infectious if a partner is in acute HCV infection. People with chronic HCV (for more than six months) are likely to have higher levels of HCV in their blood than their semen.

At least one study has reported high levels of HCV in rectal fluid.

Some recreational drugs, sharing toys and lube, rougher anal sex, fisting, and group sex are linked to higher HCV risk.

Because HCV is so much more infectious than HIV, it is more easily transmitted during group sex. Rougher, longer sex, increases the chance of bleeding.

In group sex, someone who fists more than one partner can transfer HCV without having become infected themselves.

Recreational drugs increase risk in at least three ways: tissue is more vulnerable to damage, sexual inhibition can change behaviour, and sex may be rougher and go on for longer.

One study also reported that sex after recent surgery or treatment for anal warts was a high risk for catching HCV. This would be an easy route for the virus to enter the bloodstream.

Other STIs, especially syphilis, are linked to acute HCV infection. Routine health checks are important to protect your health and that of your partners.

ChemSex

The three recreational drugs commonly referred to as ChemSex have often been reported as being linked to sexual HCV transmission.

These three drugs are crystal meth, mephedrone and GHB/GBL: “meth, meph and G”.

Compared to other recreational or party drugs, ChemSex drugs keep people high for much longer, often for several days.

These drugs are used in an almost exclusively sexual context. ChemSex has therefore been linked to high rates of STI transmission, including HIV and HCV.

PrEP and HCV

PrEP is a way for to HIV negative people to use oral HIV meds to dramatically reduce the risk of becoming HIV positive – even when not using condoms.

Although PrEP is highly effective against HIV – more than 99.9% when taken as prescribed – it doesn't protect against other STIs, including HCV.

Several PrEP studies, including UK-based, reported HCV transmission in gay men. Where HCV is a concern, condoms are likely to provide some level of protection and are therefore still recommended in UK guidelines.

HCV and pregnancy

ART is now recommended for all HIV positive people, including during pregnancy.

As well as being better for the mother's health, it dramatically reduces the risk of transmitting both HIV and HCV to the baby.

Overall, this risk of HCV transmission during pregnancy is 3% to 5%, but it is 3 to 4 times higher if the mother is HIV positive and not on ART.

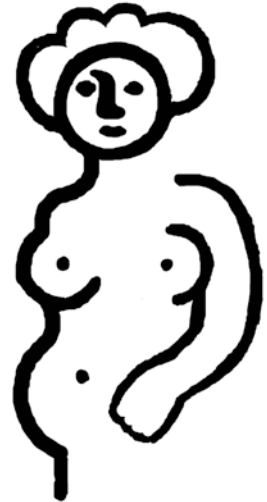
Hopefully, new HCV DAAs will be safe and effective during pregnancy, but more information is needed before they can be recommended. The old HCV drugs (pegylated interferon and ribavirin) cannot be used during pregnancy, because ribavirin causes birth defects, and interferon can cause brain and nerve damage in infants.

Women of childbearing age who have HIV/HCV coinfection should therefore have early access to HCV treatment.

HCV increases the risk of gestational diabetes, and liver damage can worsen during pregnancy. HCV also increases the risk for pre-term delivery, low birth weight and overall health (Apgar score), birth defects and infant mortality.

Guidelines for HIV positive pregnant women recommend:

- ART during pregnancy (as for HIV positive women without HCV).
- Counselling for women on ART with coinfection about signs and symptoms of liver toxicity. Liver enzyme tests are recommended one month after starting ART, and then every three months.



- HCV screening for each pregnancy.
- Screening for hepatitis A (HAV) and hepatitis B (HBV). This is because of increased risk of complications during pregnancy. HAV and HBV vaccinations after the first trimester are recommended in all susceptible women with HIV/HCV coinfection. An extra vaccine dose may be needed if the CD4 cell count is below 300.
- If the mother is on ART, UK guidelines recommend vaginal delivery, unless there are complications that need a C-section.

For more information

i-Base Guide to HIV, Pregnancy and Women's Health (2015).

<http://i-base.info/guides/pregnancy>

BHIVA guidelines for the management of HIV infection in pregnant women (2014).

<http://www.bhiva.org>

Natural history of HCV

What does your liver do?

Your liver is an essential organ that has hundreds of jobs, including:

- Filtering chemicals and waste from the blood.
- Storing vitamins, minerals and iron and converting nutrients from food into energy.
- Helping to balance levels of sugar and hormones.
- Producing cholesterol.
- Making bile (needed for digestion), and creating the hormone that helps to produce platelets (to stop bleeding).

How does HCV damage your liver?

HCV does not directly damage your liver. It is the way that the immune system reacts to the virus that causes liver inflammation.

As the immune system attempts to surround and isolate infected cells to protect the liver, scarring develops and worsens.

As the liver becomes more scarred it hardens, making it more difficult for blood and other fluids to flow through it.

Even though the liver can still work when it is damaged, the continuous effect of HCV can slowly interfere with liver function. Complications develop when the liver is too damaged to be able to carry out important tasks.

Without treatment, HCV is linked to a long list of serious complications, although many of these only occur in late stage infection.

HCV outside of the liver

As with HIV, HCV increases the risk for other health problems, including type 2 diabetes, kidney and heart disease, and bone loss. The reasons for this include inflammation from untreated HCV, long-term use of some HIV drugs, family history and lifestyle.

For people with coinfection, being cured from HCV lowers the risk for liver-related illness and death, AIDS-related illness and death, and type 2 diabetes.

Natural history of HCV

The natural history of an infection is the term for describing what happens if the infection is not treated.

The natural history of HCV infection includes three possible stages:

- Acute infection.
- Chronic infection.
- End stage liver disease (ESLD).

Glossary

acute HCV Having HCV infection for less than 6 months.

chronic HCV Having HCV infection for more than 6 months.

Acute infection

Acute infection refers to the first six months after HCV infection.

Unless it causes symptoms (and about 80% of people do not have symptoms) acute HCV is rarely diagnosed.

Symptoms, when they do occur, include fever, fatigue, abdominal pain, nausea, vomiting, dark urine, pale faeces and jaundice.

In HIV positive people, acute HCV infection is generally detected because of routine monitoring on ART. One sign of acute HCV is very high liver enzymes, sometimes 10 times higher than normal. This should prompt checking for acute HCV.

HIV positive gay men should have an annual screen for HCV, and be tested if they have been at risk. People who have cleared HCV or been cured by treatment should be screened using an HCV RNA viral load or HCV core antigen test.

In the first months after infection, some people clear HCV without treatment.

This is called spontaneous viral clearance. It is more common if:

- You had symptoms during acute HCV.
- You are female.
- You are under 40 years old.
- You have certain genes.
- Your CD4 cell count is high.

HIV positive people are only half as likely to spontaneously clear HCV as HIV negative people.

People of African descent are less likely to clear HCV than Caucasians.

Genetics are part of the reason for these differences, but other factors are also involved.

People who clear HCV without treatment are no longer infectious. They usually test positive to an HCV antibody test, but HCV will not be detectable in blood.

Whether or not to treat acute infection is complicated by three medical factors.

1. Waiting to see whether HCV clears naturally without treatment.
2. Whether you are worried about transmitting HCV to sexual partners.
3. The difference between access to old compared to new HCV drugs.

Currently, main guidelines disagree.

Some guidelines (including from the European Liver Association, EASL) recommend using DAAs in acute infection, even though these drugs are only approved for chronic infection.

UK guidelines – due to be updated – still recommend treating acute HCV with old HCV drugs (pegylated interferon and ribavirin). These drugs would not now be used.

Treating acute infection is discussed in more detail on page 34.

Link

European Liver Association (EASL) guidelines for treating hepatitis C

www.easl.eu

Chronic infection

Chronic infection refers to any time after acute infection (the first six months after infection).

In HIV negative people, untreated HCV usually progresses very slowly, often over decades.

Some people never develop serious liver damage or symptoms. But most people will have mild to moderate liver scarring (fibrosis) or symptoms such as fatigue, depression and confusion. Untreated HCV can also cause other health problems.

HIV increases the risk for, and speeds up the rate of liver damage from HCV. This is why access to DAAs may be easier for people with coinfection.

Currently in the UK, people with pre-cirrhosis and cirrhosis are getting DAA treatment. But it is important to be treated before serious liver damage develops.

Treating (and curing) HCV before HCV causes serious liver damage prevents liver failure and liver cancer.

People with cirrhosis need to be treated by a liver specialist. Although DAAs do not work as well for people with cirrhosis, the cure rate is at least 80%.

The risk for liver cancer remains high for people with cirrhosis, even after being cured and requires continued screening.

HIV and HCV coinfection

HCV is not thought to worsen HIV, but untreated HCV can make HIV treatment more complicated.

This is mainly because the liver processes most HIV drugs and HCV increases the risk for liver-related side effects from HIV drugs.

However, the benefit of HIV treatment still outweighs this risk.

Factors that speed up HCV progression include:

- HIV coinfection.
- Daily alcohol intake, especially more than 50 grams (6 units) per day.
A pint of standard strength lager is 2.3 units. A small (175 mL) glass of wine is 2 units.
- Ageing (over 40).
- Duration of HCV infection.
- Older age when infected with HCV (over 40).
- HBV coinfection.
- HCV may progress faster in men than premenopausal women.

Because DAAs are so effective, safe and they work equally well for HIV positive people, HIV/HCV coinfection should be treated.

However, many people have lived with HIV and HCV for many years. During this time, HCV may have progressed, especially if the CD4 count ever dropped below 200.

Also, some coinfection-related deaths are due to late HCV diagnosis, or late HCV treatment after severe liver damage has already occurred.

How can I protect my liver?

The easiest way to limit and prevent liver damage is to treat HCV with modern DAAs.

These drugs are safe and very effective, but high DAA prices has limited access to HCV treatment for some people.

While you are waiting for HCV treatment, you can support liver health with regular monitoring with your doctor. The following lifestyle changes can really help.

Lifestyle changes: diet, exercise, alcohol

Things that are good for your general health like reducing or stopping drinking, a balanced diet, keeping active and not smoking, are also good for your liver.

These and other changes include:

- Drink less, or stop drinking alcohol. The less you drink, the better for your liver.
- Get vaccinated against hepatitis A and B.
- A good diet includes eating less salty processed food, and more fresh fruit and vegetables, complex carbohydrates (whole grains, breads, rice, pasta), food that is low in fat and high in fibre and an adequate amount but not excessive amount of protein.



- Maintain a normal weight; being overweight increases your risk for fatty liver.
- Drink plenty of water to help your liver filter waste and toxins.
- Three cups of coffee (with or without caffeine) a day can delay fibrosis progression and lower the risk of liver cancer.
- Eating dark chocolate (85% cocoa) every day has been linked to better liver health and reduced risk of heart problems.
- Ask questions and get support. Talk with other people who are living with HCV or coinfection.

The online version of this guide includes more detailed information about diet, exercise, reducing alcohol and other lifestyle changes.



“I can’t believe how easy the DAA treatment was to take.

I continued working throughout (with a grueling schedule) and felt fine.’

After treatment, now that I’ve cleared HCV, the first time in years I’m free of daily muscle pain.

I have more energy, can concentrate better – and I no longer get hangovers!”

– Kate

Finding out you have HCV – and getting support

Finding out you have HCV

Your response to dealing with HCV might vary depending on whether this is a recent or long-standing diagnosis, and whether or not you have been HIV positive for a long time too.

It is never great news to find out you have an infection. If both diagnoses are new, then getting support for HIV might be more important than for HCV. Or if you have been HIV positive for a long time, some of ways you coped with HIV might help you now.

Whatever your circumstances, it is likely to help to be able to talk about how you feel. Often, connecting with people who have gone through similar experiences can help.

The Hepatitis C Trust:
helpline and support groups

020 7089 6221

Monday to Friday,

10.30 to 4.30pm

Calls charged at the national rate.

The Hepatitis C Trust run support groups that are women-only, men-only and mixed.

They also run a group for people with coinfection.

For information on support groups:
<http://www.hepctrust.org.uk>

Acute hep C in gay men

Since 2005, most cases of acute HCV in HIV positive people have been among gay men.

The majority of these cases occurred from sexual exposure. This raised new issues of disclosure that was often difficult because of prejudice and fear over HCV.

Although early treatment can cure HCV and reduce further transmission, access to DAAs might take time. Also, being cured once does not protect against HCV reinfection. Access to free DAAs in the UK after HCV reinfection is unlikely.

More information about the experience of gay men who have been recently diagnosed is included online.

<http://i-base.info/guides/hepc/new-infections-and-gay-men>

Long-term HIV/HCV coinfection

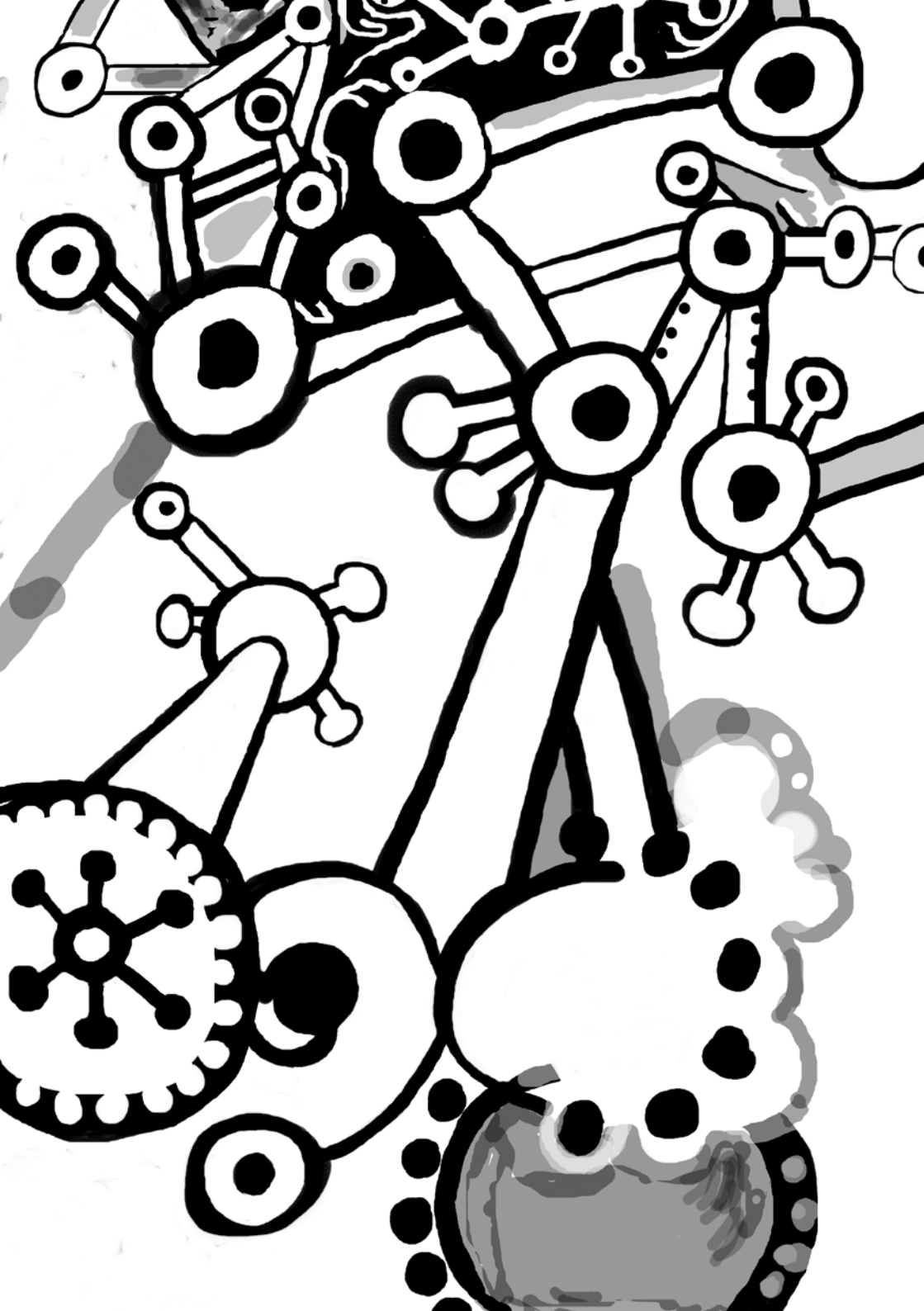
It is common for people who became HIV positive through blood products or injecting drug use to also have HCV.

Importantly, DAAs mean that most people with long-term HCV can now be cured.

Having long-term coinfection might help you access DAAs early on. Please talk to your HIV doctor about this.

More information about the experience of people with long-term coinfection is included online.

<http://i-base.info/guides/hepc/long-term-coinfection>



Testing and monitoring

HCV testing if you are HIV positive

If you are HIV positive, annual HCV testing is recommended in the UK as part of your routine care.

But HCV testing is also based on your risks. For example, if you are sexually active and/or if you have another STI and/or if you shared anything when injecting drugs then HCV tests are more important.

HCV testing is also recommended if your liver enzymes become raised.

Tests to diagnose HCV

HCV testing has two stages, but depends on your HCV history, see Table 1.

- 1) The first test is usually an HCV antibody test.

A positive antibody result means that you have either had HCV and cleared it or that you still have HCV.

A negative result means that you might not have HCV. This test doesn't detect recent HCV because it can take 6 to 24 weeks for HCV antibodies to develop.

Also, if your CD4 count is less than 200 your immune system may not make HCV antibodies.

If you have already had HCV and cleared it or been cured, routine testing (for reinfection) needs to be with an HCV viral load or HCV core antigen test.

- 2) An HCV viral load (RNA) or HCV core antigen test will confirm or rule out current infection.

These tests look for direct evidence of the virus or viral replication.

If the results are positive it means that you have current HCV infection.

If the results are undetectable/negative, you might have spontaneously cleared HCV – but a second test six months later will confirm this.

The HCV core antigen test is a cheaper and quicker alternative to HCV viral load but that gives similar information. It looks for a protein produced by ongoing HCV, but is not always accurate if HCV viral load is very low.

Table 1: HCV tests and what the results mean for HCV infection

| | Type of test | | |
|------------------------|--|---|--|
| Diagnosis | Antibody test result | HCV RNA (viral load) or HCV core antigen | ALT: liver enzyme |
| Prior HCV but cleared. | Positive. | Undetectable or negative on two tests, at least 6 months apart. | Return to normal. |
| Acute HCV. | Negative; but positive within 6 to 24 weeks. | Detectable within 1 to 2 weeks, usually very high. | May be up to 7 to 10 times above normal. |
| Chronic HCV. | Positive. | Detectable. | May be persistently normal, fluctuate, or persistently raised. |

Other routine blood tests

After an HCV diagnosis, your doctor should run other blood tests.

The most important of these are HCV genotype, liver enzyme tests (ALT/AST) and a non-invasive scan (see below).

Testing for hepatitis A and B is important so that you can have these vaccinations, if needed.

Other monitoring includes a complete blood count (CBC), blood clotting time and other liver enzymes (including albumin and GGT), kidney function and pregnancy. Information on these other tests is in the online version of this guide.

www.i-Base.info/guides/hepC

HCV genotype

There are at least seven different types of HCV, known as genotypes.

Genotypes are numbered from G1 to G7, in the order that they were discovered.

These genotypes also have variations, called subtypes, which are named by lower-case letter (i.e. a, b, c, etc), also in the order that they were discovered.

Each genotype and subtype is a distinct virus. You can be infected and reinfected by more than one genotype or subtype.

You can also be reinfected with the same or a different genotype after successfully clearing or being cured of HCV.

In the UK, everyone with coinfection should have an HCV genotype test. Although some DAAs work for all genotypes, knowing your genotype is still important.

Liver enzyme tests: ALT and AST

Liver enzymes are proteins with specific functions (and difficult long names).

If the liver becomes damaged, some of these enzymes leave the liver and enter the blood.

Many things can cause liver enzyme levels to increase. These include:

- Prescription and over-the-counter medicines.
- Herbs, vitamins and supplements.
- Toxic fumes.
- High alcohol intake or coming off drugs and/or alcohol.
- New or existing hepatitis infection.

HIV drugs can cause liver enzymes to increase, though usually not to dangerous levels. In some cases, these drugs need to be stopped or switched.

People taking HIV drugs (or other drugs processed by the liver) need to have liver enzymes routinely measured with other blood tests. This is especially important with HCV coinfection.

Raised liver enzymes do not always mean there is liver damage. But persistently high levels can be a sign of ongoing damage that needs to be treated.

Measuring liver damage

Liver damage used to be defined in two ways, based on liver biopsy results.

- 1) The “stage” measured the amount of fibrosis (scarring).
- 2) The “grade” measured the amount of inflammation, which is related to the rate of future liver scarring.

In 2017, non-invasive scans like FibroScan just report liver damage as mild, moderate or severe.

Liver stiffness (FibroScan)

In the UK, scans such as FibroScan are recommended for monitoring liver health in people with coinfection.

This scan is painless: zero pain and zero risk. It takes less than ten minutes and produces immediate results. FibroScan has dramatically reduced the need for having a liver biopsy.

FibroScan assesses liver stiffness by measuring how quickly vibration waves pass through the liver. The more damaged or stiff the liver, the more rapidly the waves will pass through it. Results are presented as a number in kilopascals (kPa). A higher number indicates more liver damage.

Results from FibroScan need to be interpreted based on other factors.

A score of over 7.2 kPa indicates higher likelihood of significant fibrosis. A score over 14.5 kPa in someone with HCV/HIV coinfection indicates cirrhosis.

FibroScan video



www.youtube.com/watch?v=I_E4ZGmKooA

i-Base FibroScan video with Dr Sanjay Baghani from the Royal Free Hospital.

However, FibroScan is not a perfect test and does not work for everyone.

- It can be too difficult to perform and results may be unreliable in people who are obese.
- It can overestimate damage in acute HCV.
- It is less sensitive at detecting small differences between mild or moderate liver damage.

However, FibroScan is very sensitive at picking up severe damage. It can therefore identify people who need HCV treatment more urgently.

If FibroScan results indicate serious liver damage, the test should be repeated to confirm the results.

Other non-invasive biomarkers

If FibroScan is not available, a panel of blood tests can sometimes be used to assess liver damage.

Combinations of lab results can help identify serious liver damage. Results are pretty good but they are not quite as useful as a FibroScan or biopsy.

In the UK, if a FibroScan is not available, or if FibroScan results are not clear, then monitoring using non-invasive blood panel tests is recommended before deciding on a biopsy.

These panels of tests include APR, FIB-4, ELF, FibroMeter and FibroTest.

Liver biopsy

A liver biopsy measures the stage and grade of liver damage by taking a small sample of liver to look at under a microscope.

However, because this is an invasive test, it is now only used when other tests are not appropriate.

The online version of this guide includes more information about liver biopsy and how Metavir and Ishak scores interpret the results.

Screening for liver cancer in people with cirrhosis

People with cirrhosis from HCV are at risk for liver cancer, even if they have been cured. Regular screening can detect early-stage liver cancer.

Usually, screening consists of a liver scan by ultrasound, computed tomography (CT) or Magnetic Resonant Imaging (MRI), and a blood test measuring alpha-fetoprotein (AFP; a protein made in foetal liver tissue).

Screening is recommended every six months.

DAAs: HCV treatment and management

Introduction to DAAs

DAA stands for direct-acting antivirals. These drugs target HCV.

DAAs cure more than 95% of people, usually from one or two pills a day for 12 weeks (but sometimes for longer).

So in an ideal world, the next step after finding out you have HCV should just be a short course of treatment. No extra monitoring or testing, just treatment and cure.

However, the high prices charged for DAAs means that access to treatment is limited for most people globally, including some people in the UK.

Different DAA classes

As with HIV drugs, each class of DAA works at a different stage of the HCV life cycle.

These classes are:

- HCV protease inhibitors (PIs).
- Non-nucleoside, nucleoside and nucleotide polymerase inhibitors.
- NS5A inhibitors.

DAAs are used in combinations, sometimes with ribavirin (RBV).

Adherence is very important with DAAs. This is defined as taking more than 95% of doses on time.

What are the goals of treatment?

There are two goals of HCV treatment.

One is to cure HCV and the other is to improve liver health.

Goal 1: curing HCV

The first goal of treatment is to clear HCV. This is called a cure.

A cure is defined as having an undetectable HCV viral load during 12 weeks after the last dose (SVR-12). SVR stands for sustained viral (or virologic) response.

Up to 99% of people who have an SVR-12 stay HCV-free. This is regardless of HIV status.

Although HCV can sometimes return after treatment is finished, this is usually within four weeks.

However, being cured does not protect you against HCV reinfection.

Currently in the UK, getting a second course of DAAs is either very limited or not available after relapse or reinfection.

Goal 2: improving liver health

The second goal of HCV treatment is to improve liver health.

This occurs from reducing liver inflammation. As well as preventing further damage, fibrosis can sometimes be partially reversed. These improvements usually happen in people who are cured.

Being cured reduces the risk of liver cirrhosis, liver cancer and liver failure in both HIV negative and HIV positive people.

In HIV positive people, a cure lowers the risk of death from liver-related and HIV-related causes, even with cirrhosis.

HCV treatment might also reduce liver-related side effects from ART.

Who needs HCV treatment?

HIV positive people with HCV coinfection should be offered DAA treatment.

But although HCV guidelines recommend everyone should be treated, access to DAAs is prioritised for people with more advanced liver fibrosis.

Since February 2017, DAAs are recommended in the UK for all genotypes. No-one should need to use the old HCV treatment with pegylated interferon (PEG-IFN) and ribavirin (RBV).

How urgently you need treatment will depend on several factors.

These factors include:

- Whether HCV is acute or chronic.
- HCV genotype can be a factor in deciding when to treat and when to wait.
- How you feel about the urgency of treatment.
- How you feel about the risk of onward transmission.
- The amount of liver damage:

Mild liver disease does not need immediate treatment. This makes it easier if you decide to wait for DAAs. Regular monitoring to assess fibrosis progression is important.

Moderate liver damage has a higher risk of progression to cirrhosis and a greater need for treatment.

Compensated cirrhosis (when the liver is damaged but can still perform) can be treated. DAAs are strongly recommended but careful monitoring is needed.

Decompensated cirrhosis (when damage is so severe that the liver stops working) can be treated with DAAs, but cure rates are lower (50% to above 80%).

Referral to a liver specialist is essential. The consultation should be about treatment, liver transplant and management of complications.

Direct-acting antivirals (DAAs)

In 2017, all guidelines recommend that chronic HCV should be treated with all oral combinations of DAAs. This includes treatment for all HIV positive people.

These drugs have high cure rates and very few side effects.

DAAs usually involve only one or two pills a day for 12 weeks. In some cases treatment takes longer.

Some DAAs are only active against certain HCV genotypes. This means that the combination that your doctor recommends will be individual to you.

Current single DAAs and fixed dose combination (FDC) tablets are listed in Table 2). Other DAAs are in development and are likely to be approved in the near future.

The online version of this table will be updated as new drugs become available.

How well does treatment work?

The high cure rates (more than 95%) shows that DAAs are effective enough to treat nearly everyone.

Even in people with cirrhosis, although cure rates are lower, they are still around 80%.

How long is HCV treatment?

DAAs generally only need treatment that lasts for 12 weeks.

The need for longer treatment depends on treatment history, sub-genotype, HCV viral load, cirrhosis and drug resistance.

Some researchers are looking at whether shorter DAA treatment might be possible.

Treatment with older HCV drugs (pegylated interferon and ribavirin) used to be for 6 to 12 months.

What about side effects?

DAAs have very few side effects. When reported, these have generally been mild and rarely involved stopping treatment.

However, your doctor needs to know about any new symptoms so that these can be checked and managed.

Side effects from ribavirin include anaemia, and feeling tired, irritable and nauseous. More information about ribavirin side effects is included in the online version of this guide.

Pegylated interferon (PEG-IFN) causes more difficult side effects. Information about these is still available online.

Table 2. DAAs, genotypes and NICE comments *

| DAA or combination ** | Class or classes | Genotypes | NICE comments for cost-effectiveness (treatment is different) § |
|---|---|-----------------------------|---|
| daclatasvir (Daklinza) Once daily. | NS5A inhibitor. | All, less data on G5 & G6. | G1: for people with pre-cirrhosis, with sofosbuvir G4: with PEG-IFN and RBV (though this combination will NOT be used). |
| elbasvir/grazoprevir (Zepatier) Once daily. | FDC: HCV protease inhibitor and NS5A inhibitor. | 1 and 4. | Cannot be used with HIV protease inhibitors or efavirenz due to drug interactions. HIV treatment needs to be temporarily changed. |
| paritaprevir/r/ombitasvir (Viekirax) with dasabuvir (Exviera) Twice daily. | FDC: boosted HCV PI/NS5A inhibitor, (with non nucleoside polymerase inhibitor (G1). | 1 and 4. | G1a, no cirrhosis: 12 weeks + RBV; with cirrhosis, 24 weeks + RBV; G1b, no cirrhosis: 12 weeks; add RBV for cirrhosis. G4: no dasabuvir, add RBV, 12 weeks; for cirrhosis, treat for 24 weeks. |
| sofosbuvir (Sovaldi) Once daily. | Nucleotide polymerase inhibitor. | All (G1, 2, 3, 4, 5, 6, 7) | Recent approvals of other DAAs mean that all oral treatments that include sofosbuvir are now available for all genotypes. |
| sofosbuvir/ledipasvir (Harvoni) Once daily. | FDC of nucleotide polymerase inhibitor/NS5A inhibitor. | 1,4, 5 and 6. | G1 (not cirrhosis): 8 weeks. G1 and 4 (naive, experienced with and without cirrhosis): 12 weeks. With cirrhosis: 12 weeks only if risk of progression is low. Longer treatment needed for decompensated cirrhosis but not funded. |
| sofosbuvir/velpatasvir (Epclusa) Once daily. | FDC: nucleotide polymerase inhibitor/NS5A inhibitor. | All. (G1, 2, 3, 4, 5, 6, 7) | NICE recommend for all genotypes, treated or untreated (except G2; only for people not cured by or who cannot use PEG-IFN). For decompensated cirrhosis, all genotypes: add RBV. |

KEY: FDC: Fixed dose combination; G: genotype; PEG-IFN: pegylated interferon; RBV: ribavirin.

* Access is more dependent on commissioning guidelines (ie NHS England or other regions).

** Simeprevir is not included due to low use. RBV is taken twice-daily.

§ See EASL guidelines (2016) for treatment recommendations by genotype.

How is the response to HCV treatment measured?

Several medical terms and abbreviations are used to describe responses to HCV treatment (see Table 3).

The most important of these is SVR-12 because this defines if HCV is cured.

Treating acute HCV

Although DAAs are not currently approved for acute infection, they are recommended in guidelines from the European Liver Association (EASL).

Cure rates are likely to be as high as for chronic HCV. SVR needs to be checked at both 12 and 24 weeks as late relapses have been reported.

If the price of DAAs limits access during acute infection, this will mean waiting for six months until HCV is defined as chronic.

Sometimes HCV will need to be chronic before you can be added to a waiting list for access to DAAs.

These guidelines and definitions might change. For example, as spontaneous clearance is very unlikely if HCV viral load does not drop within three months of infection, earlier access to DAAs might be approved in the future.

For most people, waiting for a few months will not affect long-term health.

It is good advice to stop drinking alcohol and to understand and reduce the risk of HCV for your sexual partners.

Table 3: Terms used to describe responses to HCV treatment

| Abb. | Term | Meaning and comment |
|-----------------------|---|---|
| SVR-12 | Sustained viral response 12 weeks after the end of treatment. | SVR-12 means having an undetectable HCV viral load 12 weeks after the end of treatment. This is considered a cure. |
| VBT | Viral breakthrough. | When viral load became undetectable during HCV treatment, but then becomes detectable while still on treatment. |
| Relapse | Relapse or relapser | When viral load becomes undetectable on treatment, but rebounds after it is stopped. |
| Treatment-experienced | Someone who has already used one or more HCV treatments. | With DAAs, treatment-experienced is defined by the previous type of treatment, i.e. protease inhibitor experienced. |

DAA's and HBV coinfection

Hepatitis B (HBV) reactivation can be a rare but serious problem during DAA treatment.

HBV that was previously resolved or dormant can flare-up, which can lead to liver failure that in very rare cases could be fatal. HBV testing is therefore recommended before starting DAAs.

Even though most HIV positive people in the UK are likely to be on treatment for both HIV and HBV, close HBV monitoring is needed during HCV treatment.

With HBV/HCV coinfection, one virus suppresses the other, with HCV usually suppressing HBV. DAAs cause a rapid drop in HCV viral load which can let HBV to reactivate.

ART in people with coinfection

The main concerns when choosing HIV treatment for someone with HCV are:

- Avoiding liver toxicity and damage from HIV drugs, and
- Awareness of drug interactions with HCV treatment.

Luckily, only a few HIV drugs increase the risk of liver complications in people with HCV. These are now either rarely used (d4T, ddI, tipranavir etc) or easy to avoid (nevirapine).

As DAAs only require a short course of treatment, any potential drug interactions are easy to avoid by changing ART during HCV treatment.

Retreating HCV

Although DAAs cure more than 95% of people (including people who were not cured by, or who could not tolerate PEG-IFN plus RBV) and 80% of people with cirrhosis, there are still some people who need retreatment.

If you did not respond to earlier, less effective treatment, retreatment with newer drugs might be more successful.

Some DAA regimens have been very effective for people who were not cured by PEG-IFN, RBV and a DAA, or certain DAA combinations.

Old HCV drugs: peginterferon and ribavirin

Please see the online version of this guide for information on old HCV drugs.

Ribavirin – still used with some DAAs

Ribavirin (RBV) is a nucleoside analogue similar to some HIV drugs (“nukes”).

Ribavirin is an oral drug, given as pills or capsules, twice daily. It is usually dosed by body weight. Brand names for ribavirin include Copegus, Rebetrol and Ribasphere.

On its own, ribavirin does not directly work against HCV or HIV. However, it improves the response to pegylated interferon (PEG-IFN) treatment. RBV is also used with some DAA combinations, especially in people with cirrhosis.

Peginterferon – not recommended in people with coinfection

Interferon is a man-made version of a chemical that your body already produces. It works directly against HCV but also stimulates the immune system to fight viruses. PEG-IFN is a weekly injection.

However, side effects can be severe and treatment takes 6 to 12 months.

First HCV protease inhibitors – boceprevir and telaprevir

Boceprevir and telaprevir were the first DAAs to be approved.

They are no longer manufactured because of too many difficult side effects.

Advanced liver disease

Management of cirrhosis

A damaged liver can still function, but cirrhosis increases the risk for liver failure and other serious and life-threatening complications.

DAAAs work, but are less effective (80% cure with cirrhosis rather than over 95%, without), and side effects can be worse.

Sometimes ribavirin is also needed, and/or treatment is longer (for 24 weeks).

A liver specialist should be consulted about HCV treatment.

Child-Pugh score

The Child-Pugh score is used to grade the severity of cirrhosis and end stage liver disease (ESLD). Some DAAs cannot be used in people with more advanced (Child-Pugh Class B or C) cirrhosis.

The Child-Pugh score is calculated based on results from several tests including bilirubin, albumin and PT and the presence of ascites and encephalopathy.

Class A and B categorise compensated cirrhosis with Class C indicating decompensated disease, see Table 4.

Table 4: Child-Pugh scores

| Grade | Score (points) | Cirrhosis |
|---------|----------------|---------------|
| Class A | 5-6 | Compensated |
| Class B | 7-9 | Compensated |
| Class C | 10-15 | Decompensated |

Glossary

ascites An abnormal accumulation of fluid in the abdomen, a sign of serious liver damage.

encephalopathy Worsening brain function or disease.

Liver transplant in people with HIV/HCV coinfection

When the liver can no longer adjust (or compensate) for damage, and liver function has become worse this is called hepatic decompensation (or decompensated cirrhosis).

Some DAAs can be used in people with decompensated liver disease. A liver specialist should oversee HCV treatment. Sometimes being cured improves liver function, but if it doesn't a liver transplant might still be needed.

A transplant is a major operation, and success rates vary. Access is also complicated by a lack of donor organs.

ART now enables HIV positive people to have a liver transplant. Centres in the UK, Spain, France, Italy and the US have all reported successful transplants in HIV positive people. Some centres have reported survival rates that are similar to HIV negative people.

Medical management remains complex because of the risk of graft rejection. Using DAAs before and after transplant reduces the risk of HCV reinfection of the new liver.

Drug interactions between drugs used to suppress the immune system after the transplant and HIV/HCV protease inhibitors need to be carefully managed.

HCV progresses more quickly in people who are HIV positive, and survival after decompensation is shorter compared to people who are HIV negative.

This makes it important for people with coinfection to be referred to transplant services at an earlier stage of disease than people with HCV mono-infection.

Only a few transplant centres perform liver transplants in people with coinfection, and referral to one of these centres is essential.

Drug interactions with HCV meds

HCV drugs can be used with many HIV meds but there are a few important potential interactions.

Your doctor needs to check for interactions with any other drugs that you take. This includes prescribed or over-the-counter meds, together with any supplements, herbal remedies and recreational or street drugs.

The online HCV drug interaction database from Liverpool University is free and easy to use.

www.hep-druginteractions.org

This frequently updated site includes interaction charts that use a traffic light summary:

- Red when drugs should not be used together because of an interaction.
- Amber for a caution or when additional monitoring is needed.
- Green when no interaction is likely.

Details on each interaction and reports can be printed for any combination.

Sometimes the recommendation is based on a theoretical risk and sometimes drug levels of ARVs will need monitoring.

EASL guidelines include a summary table of interactions between HCV and HIV meds.

The prescribing information leaflet (called the SPC) for each HCV drug also details drug interactions.

Links

Full prescribing information and patient information for each DAA.

i-base.info/daa

EASL clinical practice guidelines: Management of HCV infection (2016).

www.easl.eu/research/our-contributions/clinical-practice-guidelines

HCV treatment and people who inject drugs

Sometimes, people who inject drugs can have difficulty getting HCV treatment.

This is even though current guidelines recommend that people who inject drugs should be treated for HCV.

Both injection and non-injection drug users have successfully used HIV and HCV treatment. This shows that concerns about adherence should not be a barrier to treatment.

So far, there is not much information with DAAs. However, a trial in people who were actively using drugs during their HCV treatment found that adherence and cure rates were similar to those of non-users.

The following suggestions may make it easier to access treatment.

- Try not to miss medical appointments. Some doctors will use this as part of the criteria for not treating your HCV.

- Do not avoid medical care just because you are using drugs.

This is especially important while you are on HCV treatment, because your doctor will need to monitor and treat your side effects.

- Find a doctor who is willing and able to work with drug users and who will treat your HCV.
- Ask other drug users to recommend a doctor – or to steer you away from one. This can be a good place to start.
- Discuss with your doctor how side effects of HCV treatment will be managed.

If you are still injecting drugs, ask your doctor or local syringe exchange programme for information on safer injection.

This will lower your risk of HCV reinfection (and other infections).

Getting DAAs: drug pricing and drug access

This guide includes many references to DAAs. These new drugs are highly effective and easy to take.

DAAs are recommended in all guidelines, including by NICE and UK commissioners, and these drugs are available free on the NHS.

However, the high price of DAAs – around £30,000 per course – prevents the NHS from treating everyone straight away.

At the current prices, it would cost more than £7,000,000,000 to treat 230,000 people living with HCV in the UK (even though many of these people are not yet diagnosed).

This would be nearly half the total NHS drug budget for all drugs, for all conditions, both in hospitals and from GPs, for the whole UK population.

So rather than universal access that could cure nearly everyone, DAAs are being given to people who have more liver damage first.

By early 2017, the NHS has already treated 10,000 people who mostly had severe liver disease (cirrhosis). Another 10,000 people should be treated by the end of 2017.

Although there are waiting lists, people with coinfection are steadily getting DAA treatment.

The risk of waiting to treat is generally low, but this is not always the case. If cost was not an issue, everyone would be treated. For example, in Australia, and Portugal, and in Egypt with generics, governments have negotiated nationally affordable prices to treat everyone.

Guidelines for access to DAAs

In the UK, NICE recommends access to DAAs based on strong evidence that treatment is highly effective and safe.

All genotypes can be treated by DAAs, and PEG-IFN is no longer recommended.

Some hospitals are restricted for how many people they can treat, but in others, access is good, especially for people with HIV/HCV coinfection.

The choice of DAAs available can vary from month to month depending on price negotiations and where you live in the UK, but all the combinations are good.

Access is perhaps most difficult for people without liver damage but who might have other symptoms – especially if they have been living with HCV for many years.

UK rationing: area and clinic

How quickly you access DAAs in the UK will also depend on where you live (which region or country) and the type of clinic that you attend.

For example, as this guide went to press, waiting times varied between different counties in the UK, and between different clinics in the same cities.

Smaller HCV networks (called Operational Delivery Network or ODN), sometimes have earlier treatment. So in England, the best availability should be in a city that is big enough for a liver unit but not so large that it gets referrals from other units.

Larger centres, where complex and cirrhotic cases are referred to, had more patients when rationing started but now have much shorter wait times. Some smaller centres are treating everyone sooner, regardless of FibroScan score.

Ask your clinic for the approximate waiting time, and how this might change. Ask whether other clinics are shorter.

Changes will continue during 2017. Some clinics might move from having a waiting list of several months to needing to find people to keep their monthly quota.

Also, anectodally, several doctors report that most people with coinfection who are in care are steadily accessing DAAs. People with long-term coinfection should certainly be prioritised for treatment, because of the higher risk for liver cancer and faster HCV progression.

However, DAA access is less good for people who disconnect from care and/or who have ongoing drug and alcohol issues

As more people are treated with DAAs, the access problem will move to harder to reach groups, the small numbers who have had DAA failure and people who become reinfected.

Campaigning for change

If you are not able to get DAA treatment, then ask why.

Write to your doctor, health commissioner and MP.

Link to or start a community campaign to keep informed on any changes.

Most of these new DAAs are not expensive drugs to manufacture.

It costs less than £100 to manufacture a course of DAAs, and yet the NHS is being charged tens of thousands of pounds.

Buying generic DAAs online

Some people are buying generic versions of DAAs instead of waiting for the NHS to provide treatment.

This can be by either visiting a country where generic drugs are available or buying medicines online.

While this might not seem fair, both approaches are perfectly legal in the UK – and are ways to get access to healthcare.

Generic DAAs are similarly effective as patented versions made by originator companies.

Table 5: Generic DAA combinations

| Drug combination | Formulation | Genotype |
|--|------------------------|---------------|
| sobosbuvir/velpatasvir | Fixed dose combination | All. (1 to 7) |
| sofosbuvir/ledipasvir | Fixed dose combination | 1,4, 5 and 6. |
| sofosbuvir + daclatasvir (+ ribavirin if treatment experienced) | Separate pills | All. (1 to 7) |

Source: FixHepC Buyers Club, March 2017 and EASL guidelines (2016)

Community websites have information about how to do this, including:

www.fixhepc.com

www.i-base.info/qa/10734

Based on current prices on the FixHepC website, the cost for 12 weeks of generic DAA treatment is about US \$1600, depending on the drugs and supplier. See Table 5.

Whether you buy meds online or visit another country, it is important to buy DAAs from a reliable supplier.

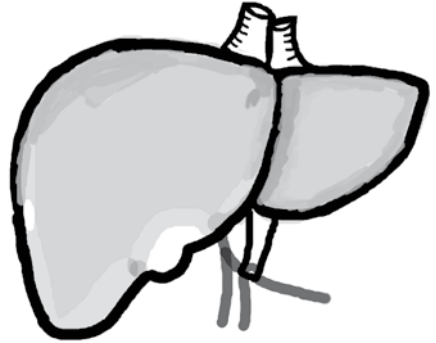
Your HIV doctor should be able to talk about which drugs would work for you. You will also need appropriate monitoring if you decide to do this. Most doctors are happy to do this, but you will need to ask.

Your doctor can also talk about the individual benefits and risks from early HCV treatment, rather than just waiting for the NHS.

Before you start HCV treatment, you and your doctor will need some basic information to pick the best treatment for you, including whether ribavirin is needed.

This information includes:

- Your general health (routine blood tests, including pregnancy testing, if indicated).
- Your HIV treatment and other medicines you are taking (to avoid drug interactions).



- Your HCV treatment history.
- Your HCV genotype (if you have genotype 1, also your subtype, which will be a letter).
- Whether or not you have cirrhosis.

This information is also important to find out how long you will need treatment – which can vary from 8 to 24 weeks.

Joining a study for access

Another way to access DAAs might be by joining a research study.

In general, drugs that are in late stage development (phase 3) already have data showing they might be as effective and safe as approved DAAs.

Many studies are looking for people with early or mild liver disease (ie who can not easily get treatment based on current UK guidelines).

Future drugs

Although DAAs work for nearly everyone, a small percentage of people need new HCV drugs.

Many other new oral HCV drugs are in development and some of these are already in advanced stage research (in phase 3 studies).

Next DAAs in advanced development

The following two fixed dose combinations (FDCs) that work for all genotypes are in late stages of development.

They are both expected to be approved (in the EU and the US) in mid-2017.

- Glecaprevir/pibrentasvir
This is a once daily, fixed-dose combination of an HCV protease inhibitor with an NS5A inhibitor.
- Sofosbuvir/velpatasvir/voipaprevir
This is a once daily, fixed-dose combination of a nucleotide polymerase inhibitor, an NS5A inhibitor and an HCV protease inhibitor.

Other triple class combinations are in earlier (phase 2) development.

Keeping up-to-date on research

A list of community organisations that report on new drugs are still in development is on page 46.

HCV treatment guidelines change when there is new information, or when new DAAs are approved.

Check them often.

Guidelines produced for Europe and the US are more likely to be updated than those produced in the UK.

EASL – European HCV guidelines

www.easl.eu

EACS – European coinfection guidelines

www.eacsociety.org

AASLD/IDSA – US hepatitis guidelines

www.hcvguidelines.org

BHIVA – UK coinfection guidelines (from 2013) are due to be updated in 2017.

www.bhiva.org

NICE – NICE publishes cost effectiveness recommendations for each new DAA that is approved in the EU.

www.nice.org.uk

NHS Scotland – updated DAA guidelines

www.hps.scot.nhs.uk/bbvsti/guidelines.aspx

Controversial issues

Price of drugs

The price of DAAs will continue to be the main barrier to widespread access and a universal cure.

This is important in the UK and it is important globally.

DAAs could make HCV an historical medical problem. DAAs are cheap to manufacture but they are priced out of reach for high, low and middle-income countries.

Drugs in development

Given the high efficacy of current drugs, additional benefits from new drugs might mainly be the impact of greater competition on drug pricing.

How long to treat

DAAs are so effective and so expensive that some studies are looking at 8 rather than 12 weeks treatment.

This seems to work best in people who do not have cirrhosis, people with lower HCV viral loads and people who have never been treated for HCV.

However, if this involves adding a third DAA, there might be little cost saving and the risk for both side effects and drug interactions will increase.

Acute infection

The balance between early treatment and waiting for six months in case of natural clearance is further complicated by DAAs not being currently recommended in acute infection. These issues might be resolved in the future.

Retreatment

There is currently little data on retreatment with DAAs in HIV/HCV coinfection.

Usually, treating people for longer, and/or with DAAs from different classes, has worked in small groups of people.

The biggest issue for retreatment is getting access to second or third courses.

HCV treatment for people who drink or inject drugs

HCV treatment is often withheld from people who use alcohol or inject drugs.

This is despite guidelines that already recommend treatment. As more people are treated and cured, and with better access to clean injection equipment, methadone and buprenorphine, the less HCV will be transmitted.

Sexual transmission

The mechanisms for why some HIV positive people have a higher risk of sexual HCV transmission will hopefully become more clear.

DAAs will reduce sexual transmissions as more people are cured. This will reduce the number of people who are still infectious. Avoiding reinfection is likely to continue to be important.

Further information

HIV i-Base

HIV i-Base is an treatment activist, advocacy and education organisation based in London, set up in April 2000.

i-Base runs a treatment information phoneline on 0808 800 6013 on Monday, Tuesday, Wednesday from 12-4pm.

i-Base publishes non-technical treatment guides, and a monthly bulletin for doctors, all of which are available free in print, and online:

www.i-Base.info

Keeping up to date with research

The following websites provide a range of information and news on the latest developments.

A wealth of reports from journals, meetings and conferences are posted on the National AIDS Treatment Advocacy Project (NATAP) website.

www.natap.org

An updated list of HCV drugs in development is available on the HCV Advocate Website.

hcvadvocate.blogspot.ca

HIVandHepatitis.com covers medical conferences and HCV-related news.

www.hivandhepatitis.com

InfoWeb: hepatitis news for advocates and people working in Europe.

www.infohep.org

Support organisations

The Hepatitis C Trust (UK)

020 7089 6221

www.hepctrust.org.uk

Antidote is a drug and alcohol service for lesbian/gay/transsexual/bisexual people, based in London with a national phoneline. 020 7833 1674 (10am-6pm, Monday to Friday).

This service includes counselling and other 1-2-1 support based at several London HIV clinics.

www.londonfriend.org.uk

www.facebook.com/antidotelgbt

Alcoholics Anonymous

www.aa.org

Narcotics Anonymous

www.na.org

Addiction Treatment Watchdog Forum

A forum for people on methadone and buprenorphine for opioid addiction.

www.atwatchdog.lefora.com

National Alliance of Advocates for Buprenorphine Treatment (US)

www.naabt.org

Methamphetamine

Crystal Meth Anonymous

www.crystalmeth.org

Harm reduction resources and forums

Harm Reduction Coalition (US)

Information and news about HCV best practices, tools and advocacy and harm reduction resources (US)

www.harmreduction.org

International Network of People who Use Drugs (INPUD)

www.inpud.net

EROWID: Information about psychoactive substances

www.erowid.org

Drugs Forum: An information hub and platform to discuss recreational drugs

www.drugs-forum.com

The Fix: addiction and recovery news

www.thefix.com



Glossary

ALT – (alanine transaminase, also called serum glutamate-pyruvate transaminase; SGPT). A key liver enzyme produced in liver cells. ALT is routinely monitored in HIV positive people on ART to detect liver toxicity from HIV drugs (or other medications). Elevated ALT signals liver injury, but does not indicate how serious liver damage is.

ascites – an abnormal accumulation of fluid in the abdomen, a sign of serious liver damage in people with HCV.

ART – antiretroviral treatment: HIV meds.

AST – (aspartate aminotransferase; serum glutamic-oxaloacetic transaminase; SGOT). An enzyme that is made in many places throughout the body (heart, intestines, muscle). AST is routinely monitored in HIV positive people on ART to detect liver toxicity from HIV drugs (or other medications). Elevated AST that is specifically made in the liver signals liver injury, but does not indicate how serious liver damage is.

biopsy – taking a small sample of body tissue to look at in a laboratory.

cirrhosis – severe scarring of the liver that reduces how well the liver works.

coinfection – infection with more than one virus

DAAs – direct-acting antivirals – new HCV drugs.

encephalopathy – worsening brain function or disease.

enzyme – a protein produced in the body that speeds-up other chemical reactions.

fibrosis – mild to moderate liver scarring.

FibroScan – non-invasive ultrasound scan that measures the elasticity or stiffness of the liver.

genotype – a category for different families of HCV.

grade/grading – the amount of inflammation in liver tissue biopsy.

hepatotoxicity – the medical term for liver related side effects.

jaundice – a common symptom of hepatitis: increased levels of bilirubin lead to a yellowing of the skin or eyes.

monoinfection – infection with one virus.

NNRTI – Non-Nucleoside Reverse Transcriptase Inhibitor (a type of HIV drug).

pegylated interferon (PEG-IFN) an old HCV drug used with ribavirin.

PI (Protease Inhibitor) – a type of HIV or HCV drug.

PWID – a person who injects drugs.

ribavirin – a twice-daily oral drug sometimes used with DAAs.

stage/staging – the stage of hepatitis refers to the amount of scarring (fibrosis), from a biopsy. It is usually measured on the Metavir scale of 0 to 4, where 0 represents no scarring and 4 cirrhosis, or on the Knodell scale of 0 to 6, where 0 is no scarring and 6 cirrhosis.

SVR-12 - sustained viral response: having a negative HCV viral load test 12 weeks after stopping HCV treatment. SVR-12 shows that HCV is usually cured.

toxicity – the side effect from treatment.

varices – extended or swollen veins that can burst, a complication of cirrhosis.

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,

107 The Maltings, 169 Tower Bridge Rd. London SE1 3LJ.

Or made directly online at: www.surveymonkey.co.uk/r/7FKRM99

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

Too easy

Easy

Difficult

Too difficult

2. How much of the information did you already know?

None

A little

Most

All

3. Did the information help you feel more confidence when speaking to your doctor?

Yes, a lot

Yes, a little

Maybe

No

4. Which information did you find most useful?

5. Do you still have questions after reading this guide? Please give examples.

Please include a contact email address if you would like us to contact you about this

6. Any other comments?

Contact details (If you would like a reply): Name _____

Email _____ @ _____



i-Base publications

All i-Base publications are available free
Treatment guides are written in everyday language
HTB is written in more technical medical language

Please photocopy or cut out this form and post to
HIV i-Base, 107 The Maltings,
169 Tower Bridge Road, London, SE1 3LJ
or fax to 020 8616 1250
or order online www.i-Base.info

Please send me

- Introduction to ART
- Changing treatment: guide to second-line therapy
- Pregnancy and womens health
- Guide to hepatitis C for people living with HIV
- HIV testing and risks of sexual transmission
- UK guide to PrEP
- HIV Treatment Bulletin (HTB)

Name

Address

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Email

Thanks to The Monument Trust and MAC AIDS Fund for funding this publication

0808
800
6013

**i-Base Treatment
information Phonenumber**

**Monday to Wednesday
12 noon to 4pm**

i-Base can also answer your
questions by email or online

**questions@i-Base.org.uk
www.i-Base.info/questions**

