

## British HIV Association (BHIVA) guidelines for the management of HIV-2 2021: non-technical summary

### The management of HIV-2

The British HIV Association (BHIVA) produces medical guidelines about HIV treatment and related topics. All guidelines make recommendations after reviewing the evidence for the best care. Although these guidelines are for clinicians, it is important that you know what is in them. This non-technical summary aims to provide the main points from the guidelines about the management of HIV-2. You can check the full guidelines for more detail at: [www.bhiva.org/HIV-2-guidelines](http://www.bhiva.org/HIV-2-guidelines).

### Key messages

- There are two main types of HIV. The most common type is HIV-1. Most people with HIV in the UK have HIV-1.
- HIV-2 is much less common. It is seen mostly in West Africa, or in people of West African origin. HIV-2 behaves differently, and is harder to monitor and treat than HIV-1.
- Some people with HIV-2 can have very low levels of virus in the blood, and their immune system can remain relatively strong for many years without treatment. This can continue for much longer than is the case for HIV-1. This might mean that they are less likely to want to start treatment. But we still suggest that everyone should start treatment for HIV-2 as soon as they are able after diagnosis.
- If you decide **not** to start treatment, you should still be monitored regularly by your HIV clinic, to see how HIV-2 is affecting your health.
- There are situations where it is important that you start treatment straight away. These include if you have increased levels of HIV-2 in the blood, signs of a weakened immune system, other infections or other underlying health conditions, or if you are pregnant.
- Treatment for HIV is called antiretroviral therapy (ART). It usually involves taking a combination of antiretroviral medications every day. These medications were all developed for HIV-1. ART for HIV-1 is very effective, and the medications used today are usually very easy to take with few if any side effects. Often, ART involves taking only one tablet, once a day.
- ART for HIV-2 is more complicated. There are some medications that cannot be used for HIV-2, so the choice is more limited. But ART for HIV-2 is still very effective and easy to take.
- Adherence (taking your medication as prescribed, on time, every time) is important to prevent HIV becoming resistant to the medications used. Resistance to some medications seems to develop more easily for HIV-2 than for HIV-1. And if resistance develops, there are fewer alternative options. So adherence is especially important for HIV-2.
- You should be given support with adherence if you need it.
- Monitoring for HIV-2 when you are taking ART is very similar to that for HIV-1.
- Treatment options for pregnant women, newborn babies, children and adolescents are more limited. Specialist advice may be needed.
- You may need more support with living with HIV-2. Peer support can be helpful. This is where others with HIV share their experience with you and offer information and support. But most peer support in the UK is from people living with HIV-1, so their experiences may be different, especially with regard to issues related to treatment. Peer support can still be very helpful for dealing with many other issues, such as stigma and adherence.

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## Introduction

There are two major types of human immunodeficiency virus (HIV). The one seen most widely in the world is HIV-1, which was the first type to be discovered. There are currently about 38 million people living with HIV in the world. This includes people with HIV-1 and a second, less common, type of HIV, called HIV-2. This is thought to affect 1–2 million people. Most of the people living with HIV-2 are in West Africa or of West African origin. In the UK, HIV-1 is by far the most common type, with about 110,000 people living with HIV-1. There are fewer than 500 people living with HIV-2 in the UK.

There are two important blood tests that are used to see how HIV is affecting your health, and how well any treatment is working. These are:

- Viral load – this shows how much virus is circulating in the body
- CD4 count – this is a measure of how well your immune system is working

There are important differences between the two types of HIV. HIV-2 is less likely to be transmitted than HIV-1 because the viral loads tend to be much lower. Also, without treatment, it takes much longer for someone to become ill with HIV-2. And HIV-2 can be harder to diagnose and treat than HIV-1. It is possible to have both HIV-1 and HIV-2 at the same time. This is called dual infection.

Most of the antiretroviral medications available for the treatment of HIV were developed for HIV-1. There have been far fewer scientific studies of treatment for HIV-2 than for HIV-1. Even so, many of the same general principles for the treatment and management of HIV-1 can be applied to HIV-2. For example, for someone who is on effective ART, undetectable equals untransmittable (U=U) will apply for HIV-2 as well as for HIV-1. U=U means that if the level of virus in your blood is very low ('undetectable'), you are not able to pass HIV on to anyone else through sex ('untransmittable').

But there are some significant differences between HIV-1 and HIV-2, and these are discussed in this non-technical summary.

## Diagnosis of HIV-2

There are different types of HIV test. Some tests detect both HIV-1 and HIV-2, but do not distinguish between them. This means that further tests are needed, specifically designed to test for HIV-1 or HIV-2, before it is clear which type of HIV is present. These tests are done routinely at diagnosis. You may need repeated tests over several months to make sure that cases of dual infection (with both HIV-1 and HIV-2) are also detected.

Other routine tests for HIV, such as viral load, need to be done in specialised laboratories for HIV-2. This means that it may take longer for you to get the results than for HIV-1.

If you are diagnosed with HIV-2, resistance testing should be done at diagnosis and before the start of any treatment. This is to make sure that the antiretroviral medications used for your treatment will be effective.

## Treatment

Because HIV-2 behaves differently, there are differences in the way HIV-2 is treated, compared with HIV-1. It is important to understand these differences.

After HIV infection but before treatment is started, blood tests for viral load and CD4 count show differences with HIV-1 or HIV-2 infection.

With HIV-1, within a few weeks of the initial infection, the viral load increases to very high levels, often millions of copies/mL. This reduces over the next few months, but usually to levels that are still quite high (thousands of copies/mL). Over several years, if the person does not start ART, the viral load then increases steadily. At the same time, the CD4 count drops initially after HIV-1 infection,

but then recovers quickly, although not completely. Without treatment, the CD4 count will then fall steadily over many years. For most people the immune system is seriously damaged after about 8–10 years, when the CD4 count becomes low. Below a CD4 count of 200 cells/mm<sup>3</sup>, there is a risk of serious illness. If the CD4 count falls below 50 cells/mm<sup>3</sup>, the risk of illness, with serious or life-threatening conditions, is very high.

HIV-2 behaves differently. After a spike following the initial infection, the viral load stays relatively low or undetectable for many years. Also, the CD4 count falls much more slowly than with HIV-1. This means that it may take much longer (maybe 20 years or more) before a person with untreated HIV-2 is at risk of serious illness because of a weakened immune system.

This non-technical summary is about the guidelines for the treatment of HIV-2, but the differences from the treatment for HIV-1 will be mentioned briefly. Separate guidelines with more detail for the treatment of HIV-1 can be found here: <https://www.bhiva.org/HIV-1-treatment-guidelines>.

### When to start treatment

For HIV-1, we recommend that everyone should start ART as soon after diagnosis as they feel able to. This has been shown to give the best outcome for future health. It is also helpful in terms of prevention, because once viral load becomes undetectable, HIV cannot be passed on through sex (U=U).

But the situation for HIV-2 is much less clear. With HIV-2, you may have an undetectable or very low viral load for many years, with a high CD4 count. There is less direct evidence to show the benefit of starting ART as soon as possible after diagnosis. So it could be possible to delay starting ART. However, there is some evidence to suggest that even though your viral load may be low and your CD4 count high, HIV-2 is still slowly damaging your immune system. There is strong evidence for HIV-1 that it damages the immune system even if the viral load is low and CD4 count high. And it seems reasonable to think that this may also apply to HIV-2. There are many antiretroviral medications available today that have very few if any side effects, so there are now fewer disadvantages of starting ART than there were some years ago using older antiretroviral medications.

If you are diagnosed with HIV-2, your healthcare team should discuss the relative risks and benefits of starting ART. We suggest that it is better for most people to start ART as soon as they are able, whether they have HIV-1 or HIV-2.

If you choose not to start ART, it is still important that you come to clinic regularly in order to see whether or not your immune system is being damaged. This is done by monitoring the HIV-2 viral load and CD4 count from samples of your blood. Typically, viral load and CD4 count should be checked every 6 months.

However, there are some circumstances where we strongly recommend that you start ART. These include:

- If you have HIV-1 and HIV-2 dual infection
- If you are diagnosed very soon after initial infection with HIV-2
- If you also have hepatitis B
- If you are pregnant
- If your HIV-2 viral load is detectable
- If your CD4 count is less than 500 cells/mm<sup>3</sup>
- If you have HIV-related opportunistic infections
- If you have other underlying health conditions

Before recommending that you start ART, your healthcare team should discuss the reasons for this with you.

### What treatment to start with

Many antiretroviral medications have been developed and approved for the treatment of HIV-1. There are over 30 different antiretroviral medications of several different types (called classes). ART for HIV-1 usually means taking two or three different medications from at least two classes. ART for HIV-1 is very effective, and usually very easy to take with few if any side effects. Often, different antiretroviral medications are combined into one tablet, taken once a day.

The situation for HIV-2 is not as clear because there have been far fewer scientific studies of treatment for HIV-2 than for HIV-1. There are no antiretroviral medications specifically approved to treat HIV-2. Our understanding of the use of these medications for the treatment of HIV-2 is based on our understanding of their use for HIV-1.

HIV-2 is naturally resistant to all the medications in the class of antiretroviral medications called non-nucleoside reverse-transcriptase inhibitors (NNRTIs), and also to another smaller class called fusion inhibitors. This means that these antiretroviral medications are not effective for treating HIV-2, and so there are fewer medications to choose from for HIV-2 than for HIV-1. There are also some concerns about how long-lasting the treatments for HIV-2 may be. HIV-2 may also more easily develop resistance to the antiretroviral medications used than HIV-1. But there are still many good treatment options for HIV-2.

For HIV-2, ART will usually mean taking three antiretroviral medications from two different classes. Adherence (taking your ART on time, every time, as prescribed) is important for the treatment of both HIV-1 and HIV-2. If you regularly miss doses, or stop your ART, the level of virus in your blood quickly rises. If the levels of antiretroviral medications in your blood are low, and there is enough virus present to multiply, then it is possible that resistance to these medications can develop. This means they stop working. This could have a serious impact on your health.

Adherence is especially important for HIV-2 treatment, because there are concerns that HIV-2 can develop resistance to some medications more easily than HIV-1. Also, there are fewer alternative antiretroviral options if you then need to change treatment. Your HIV healthcare team should discuss how best to take your ART, and offer you any support you might need to be sure that you can take it on time, every time.

Your HIV healthcare team will make recommendations on which antiretroviral medications to take, based on the results of your resistance tests and your particular circumstances.

### Monitoring

Some people diagnosed with HIV-2 may have undetectable viral loads and high CD4 counts for many years after diagnosis without treatment. They may choose not to start ART. But it is still important to check how HIV-2 is affecting the immune system. This is done by measuring CD4 count, usually every 6 months, to be sure that it does not fall to low levels. Viral load should also be measured, to see whether or not there is an increase in the level of HIV-2 in the blood.

If you are on ART and your viral load is undetectable, then you cannot pass HIV on through sex (U=U). If you have been diagnosed with HIV-2, and your viral load is undetectable but you are **not** taking ART, it is not clear whether U=U applies. So we recommend that you should take the usual precautions to prevent passing on HIV to others. You should not rely on U=U alone.

If you are on ART, your health will be monitored using blood tests to make sure that the HIV treatment is continuing to work well. As well as viral load and CD4 count, many other tests will be

done routinely to check that your overall health is not being affected by either HIV or ART. You will typically need to come to clinic every 6 months, but maybe more frequently immediately after your initial diagnosis. Monitoring for HIV-2 will be broadly similar to the monitoring that is done for HIV-1. There are full details of this in separate guidelines: <https://www.bhiva.org/monitoring-guidelines>.

### **Pregnant women, newborn babies and children**

If you are diagnosed during pregnancy and not already taking ART, we would recommend starting ART, even if your HIV-2 viral load is undetectable. There are fewer ART options for HIV-2 for pregnant women, so advice from specialists in the treatment of HIV-2 during pregnancy may be needed to find the right ART option for you. But there are still good treatment options available. Not only will starting treatment be better for you, but it will also reduce the risk of your baby being born with HIV-2 (this is called vertical transmission). You should continue to take ART after the birth of your baby.

We suggest that your newborn baby should also have a short course of ART, typically for 2 to 4 weeks. Your HIV healthcare team should seek expert advice on how best to do this.

There is more information about the management of HIV during pregnancy and after giving birth in separate guidelines: <https://www.bhiva.org/pregnancy-guidelines>.

There are very few children living with HIV-2. And there is very little evidence to suggest how best to treat children. Because of this, the healthcare of children and adolescents living with HIV-2 will be reviewed carefully by a multidisciplinary team, to ensure they get the best possible treatment and care.

### **If treatment stops working**

There may be occasions when the monitoring tests show that even though ART has been started and is continuing, the viral load is increasing steadily, or the CD4 count continues to fall. If this happens, your HIV healthcare team will try to understand the cause, and how best to resolve it. This may mean taking blood samples for resistance testing. But in many cases this situation may have arisen due to difficulties with adherence. It is important that you are honest with your healthcare team about how you are taking your treatment. If you are struggling to take your ART on time, every time, then you should be given advice and practical support to help you. It may be that you also need to change the antiretroviral medications that you are taking or you may need to take more than the usual three medications, to try to reduce the viral load to undetectable levels.

### **Supporting people living with HIV-2**

HIV-2 is more difficult to diagnose, monitor and treat than HIV-1. The situation can seem more uncertain, and more complicated. Your HIV healthcare team should provide enough information about your treatment, and involve you as much as you want in your treatment decisions. But there are a lot of uncertainties, and you may find this emotionally challenging. Your healthcare team should provide you with support if you feel you are struggling with your emotional or mental well-being.

Adherence is particularly important for HIV-2, and this should be clearly explained to you. You should also be offered support for this, if needed. We know that most people with HIV-2 live long and healthy lives on ART, just like those with HIV-1.

There are many organisations in the UK that offer HIV information and peer support. Peer support is where you are able to share your experience with others who are also living with HIV, and receive practical and emotional support. This can be extremely helpful in dealing with many of the issues associated with HIV, such as stigma. But most HIV support organisations in the UK have little or no

experience of HIV-2, so the experience that people have may not reflect the situation with HIV-2, particularly relating to treatment issues. Nevertheless, they may still be able to help with a wide range of other issues, including adherence support.

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### Further information and support

Community organisations in the UK that produce information and resources about HIV treatment include HIV i-Base (<https://www.i-base.info>), Terrence Higgins Trust (<https://www.tht.org.uk>) and NAM (<https://www.aidsmap.com>).

### About BHIVA

The British HIV Association (BHIVA) is an organisation for health professionals in the UK. Members include doctors, nurses, researchers, pharmacists and community advocates. Since 1995, BHIVA has been committed to providing excellent care for people living with and affected by HIV. BHIVA is a national advisory body on all aspects of HIV care and provides a national platform for HIV care issues. To help promote and monitor high standards of care, BHIVA publishes a range of clinical guidelines: <https://www.bhiva.org/guidelines.aspx>.

Information about how BHIVA guidelines are developed can be found at: <https://www.bhiva.org/clinicalguidelines.aspx>.