Public Health England

16th May 2014

Frequently Asked Questions on HIV & HIV Testing: Resource For 3Cs & HIV Programme Trainers

BACKGROUND

This FAQ document is intended to support the delivery of the HIV testing component of the 3Cs & HIV programme, by providing trainers with additional background material on the treatment of HIV and the natural history of HIV infection . It also includes responses to recent questions on HIV testing that have been raised during the course of the programme. This material is for trainers to use as they feel appropriate, and it is not necessary to incorporate it into the 3Cs & HIV training.

HIV TREATMENT

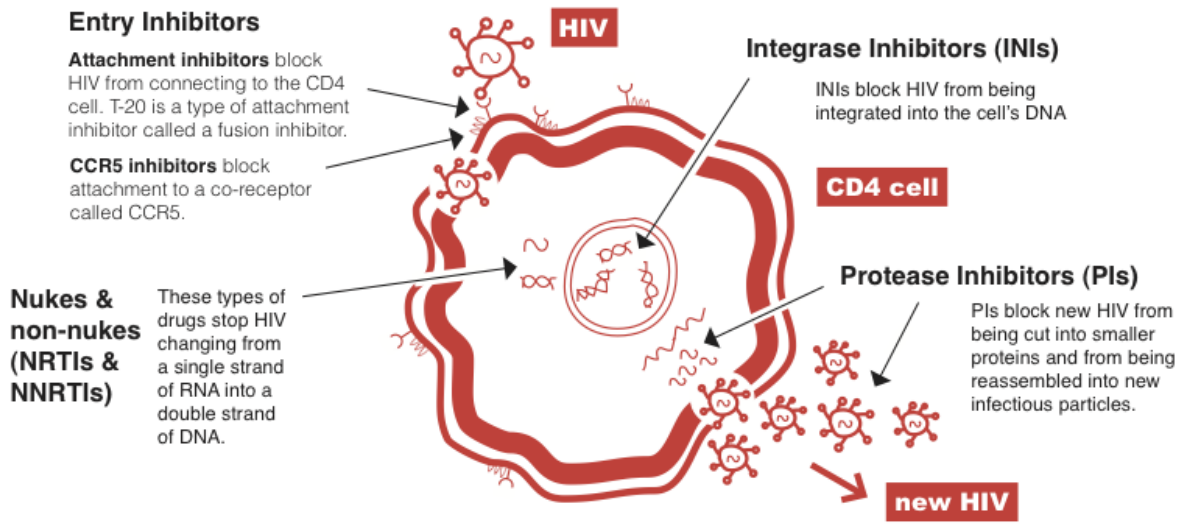
1. How does HIV treatment work?

HIV is treated with antiretroviral drugs (ARVs), which work against the HIV infection by preventing the virus from making copies of itself Patients usually take three or more types of ARV medication, which can be delivered by a single tablet regimen. This is known as combination therapy or antiretroviral therapy (ART).

The main classes of ARVs are as follows:

Class	Also known as	Mechanism	Examples
Entry inhibitors	Fusion inhibitors, attachment inhibitors, CCR5 inhibitors	Interferes with binding, fusion and entry of HIV-1 to the host cell	T-20, maraviroc
Reverse transcriptase inhibitors	NRTIs, NtRTIs, NNRTIs,	Prevents the virus from converting its genetic material into DNA after it has entered the cell	Efaverenz, abacavir, tenofovir, 3TC, AZT, FTC
Integrase inhibitors	INIs	Prevents the virus from being integrated into the genetic material of the host cell	Raltegravir
Protease inhibitors	PIs	Prevents the virus from successfully budding off and spreading from infected cells.	Darunavir, atazanavir

This diagram shows the stages of the virus lifecycle targeted by each class of ARVs:



Source: *Introduction to combination therapy,* HIV i-Base 2013[1]

2. What is the recommended first line treatment for HIV?

Patients who have not been on HIV treatment before should start on a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) and one drug from another class: a protease inhibitor, an integrase inhibitor or a non-nucleoside reverse transcriptase inhibitor (NNRTI).

BHIVA guidelines set out a preferred set of specific drugs, which are strongly recommended based on the best available evidence. They provide an alternative set of drugs, which are also acceptable and may be the best option based on certain factors, such as side effects or medical history.

These sets of drugs for first-line treatment are listed below:

	● Preferred	○ Alternative
NRTI	*Truvada* This is tenofovir and FTC (emtricitabine) combined in one tablet	*Kivexa* This is abacavir and 3TC (lamivudine) combined in one tablet
Third drug	Atazanavir* (*Reyataz*) Darunavir* (*Prezista*) Efavirenz (*Sustiva*) Raltegravir (*Isentress*)	*Kaletra* (lopinavir/ritonavir) Fosamprenavir* (*Telzir*) Nevirapine (*Viramune, Viramune prolonged-release*) Rilpivirine (*Edurant*)
*These drugs are boosted with another protease inhibitor, ritonavir (*Norvir*), to boost their levels in the body.		

Source: *HIV treatment for adults: starting treatment*, BHIVA 2013[2]

3. When should someone go on treatment?

People should start HIV treatment when their CD4 cell count (a measure of the strength of their immune system) is at or less than 350. Treatment should be started earlier if patients are older, have an AIDS-defining condition such as pneumonia, have co-infection with hepatitis B or C, or are on radiotherapy or chemotherapy that would suppress their immune system. Patients may also wish to start treatment earlier to reduce the chances of them passing on HIV to their sexual partners.

Patients should be given the opportunity to be involved in the decision about when to start treatment. This should follow a discussion with their HIV clinician about the pros and cons of starting HIV treatment, and the treatment options available to them.

4. What is the long-term outlook for someone on treatment?

The introduction of effective ART transformed in 1995 transformed HIV from a fatal infection to a chronic, manageable life-long condition. People living with HIV can expect a near normal life span and good clinical outcomes as long as they are diagnosed promptly after infection.

5. What side-effects can result from treatment

Side effects from modern HIV drugs are usually mild, and can be often be reduced by use of pre-emptive additional medication or by switching to other drugs. The most common side effects include nausea, diarrhea and tiredness, and one of the most common drugs (efavirenz) can cause changes to mood and sleep patterns. These side effects often reduce in severity after the first few weeks on treatment.

Notable previous side effects of HIV treatment were lipodystrophy and lipoatrophy, meaning changes to the distribution of body fat over a period of several months. These changes are now seen less frequently with modern HIV drugs.

HIV NATURAL HISTORY

6. What are the initial symptoms of HIV infection?

Early (or primary) HIV infection can cause a range of symptoms, which can be very similar to the flu or other common viral illnesses[3]. These symptoms are sometimes called seroconversion illness, and occur in as many as 90% of those diagnosed with HIV. Although many people seek medical care for these symptoms, the diagnosis of HIV is often missed due to the similarity with other illnesses.

Symptoms can include: fever, rash, headache, feeling generally unwell, aches and pains, mouth ulcers, sore throat, night sweats, weight loss, tiredness, swollen glands, and neurological symptoms such as meningitis. Symptoms typically appear a few days to a few weeks after exposure to HIV and can persists for two to four weeks, although swollen glands may last longer.

Although some modern HIV tests can detect infection much earlier than previously, in very recent infection the test may be negative due to a window period in which infection is not detectable. In this scenario, if primary HIV infection is suspected, either urgent referral to specialist GUM services or a repeat test in seven days is recommended.

7. What is the natural history of infection if not treated?

After the first few weeks of HIV infection, in which symptoms are often present and the levels of virus in the blood are high, the immune system begins to mount a response, so that levels of virus in the blood decline and symptoms disappear. Antibodies to HIV typically appear four to six weeks after infection, but may occasionally take as long as twelve weeks.

There follows a latent period during which the immune system and viral replication are in balance, and there are few or no symptoms of HIV infection: during this time the virus is still replicating, but controlled by the immune system. The length of this latent period varies from individual to individual, but typically lasts for less than ten years after infection.

Over time the immune system is no longer able to fight the virus as effectively. The amount of virus in the blood increases and the number of immune cells in the blood declines. Eventually the

immune system is no longer able to resist opportunistic infections, such as pneumonia, , and the patient progresses to acquired immunodeficiency syndrome (AIDS). Without treatment, the frequency and severity of infections increases over time, as does the risk of developing viral-induced cancers, eventually resulting in death. The mean survival time after diagnosis of AIDS prior to the availability of antiretroviral treatment was 10-12 months.

Over three quarters of those living with HIV in the UK are aware of their infection, and therefore able to access treatment before progressing to AIDS. However those who are diagnosed late (i.e. after being infected for several years) have a ten-fold increased risk of death in the first year of diagnosis compared to those diagnosed early.

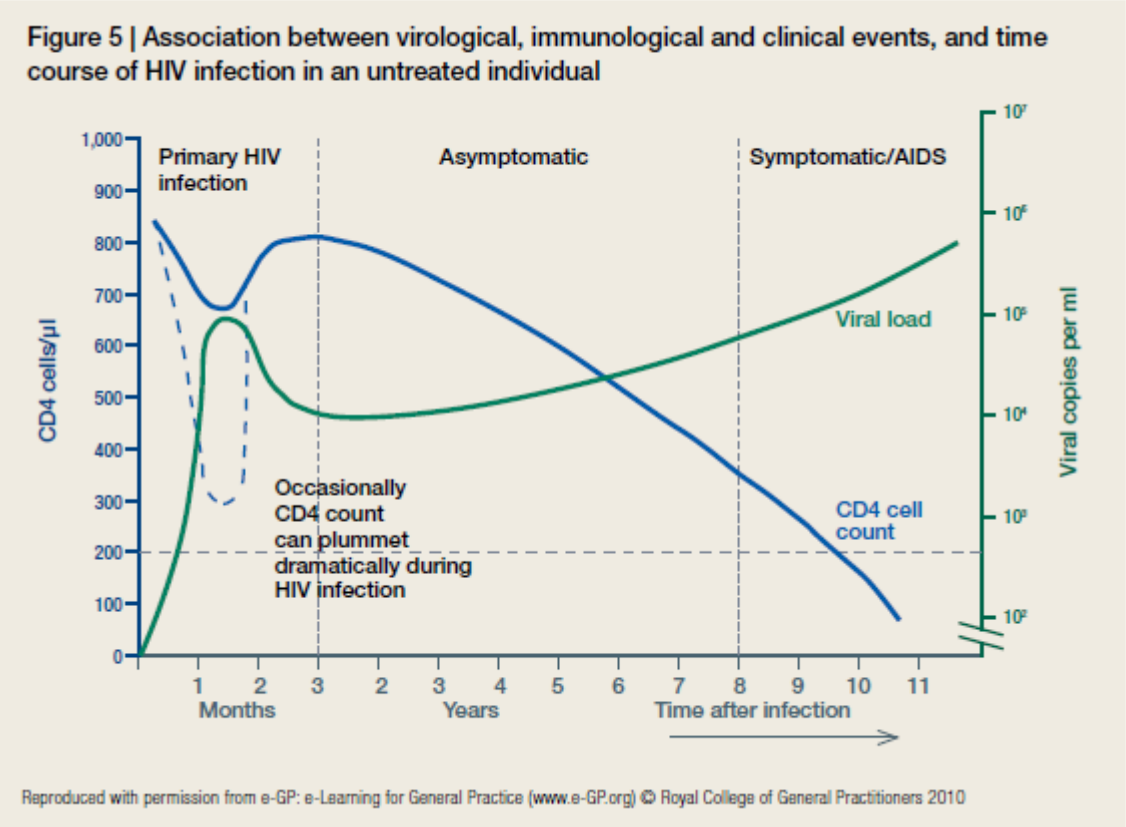


Figure 5 | Association between virological, immunological and clinical events, and time course of HIV infection in an untreated individual

8. What do CD4 and viral load mean?

CD4 cells (sometimes called T-cells, or helper cells) are white blood cells that organise the immune system's response to infections. CD4 test results are a (surrogate) measure of the patient's immune system, and are used to help decide when someone should start HIV treatment. Results are given as number of cells per cubic millimetre (mm3).

A CD4 count of between 500 and 1500 is considered 'normal', and around 350 or lower is typically when UK guidelines recommend starting treatment[4]. Patients who have a very low (<200) CD4 count when diagnosed are likely to have been infected for several years (i.e. are diagnosed late) and are vulnerable to opportunistic infections, but should recover when placed on treatment. Low CD4 counts are also seen in patients who have been recently infected.

Viral load (VL) tests measure how much virus is in a small sample of blood. This is used to monitor how well a patient's treatment is working. Results are given as copies/mL.

The aim of treatment is to reduce VL to the point where it is 'undetectable', i.e. less than 50 copies/mL, and keep it there: this is a sign that the treatment is working. If this does not happen, or the viral load increases over time, this may indicate that the drugs aren't working as expected or that the patient isn't taking their medication correctly[5].

It's important that people with HIV have regular blood tests to monitor both CD4 and viral load, regardless of whether they are on treatment. According to BHIVA standards of care, a full assessment including blood tests should be taken soon after diagnosis. After this, blood tests should be taken at least once every three months, eventually reducing in frequency to every six months if the individual is considered to be stable and free of symptoms.

9. How do mortality rates for individuals with HIV compare to the general population?

Rates of HIV-related mortality have dramatically decreased since the introduction of effective HIV treatment in the mid-1990s. All-cause mortality among people with HIV aged 15-59 years in England and Wales between 2002 and 2012 declined from 15 per 1,000 in 2002 to 4.5 per 1,000 in 2012. This compares to a mortality rate of 1.5 per 1,000 in the general population in 2012. Mortality rates were higher among men (4.9 per 1,000) compared to women (3.8 per 1,000); in the general population, this was 1.8 per 1,000 and 1.2 per 1,000, respectively for the same year.

HIV CLINICAL INDICATORS

10. What are the clinical indicators of HIV infection?

Patients may present to primary care with a wide variety of conditions that can suggest underlying HIV infection: some of these are relatively common among the general population but more common among those with HIV (e.g. herpes zoster), and some are very specific to people with HIV or AIDS (e.g. Kaposi's sarcoma).

Indicator conditions are those that occur more frequently in HIV positive persons either because they share the same mode of transmission (e.g. STIs) or because they can occur due to the immune deficiency associated with HIV infection. A reference sheet of the conditions when HIV testing should be routinely offered was provided in the trainer's pack.

The Medical Foundation for HIV and Sexual Health (MEDFASH) document *HIV in Primary Care* (2011) describes the presentation of these indicator conditions in detail[6].

11. Is further information available on the three clinical indicator diseases given as examples in the 3Cs & HIV presentation?

The HIV testing training for the 3Cs & HIV programme gave the example of three indicator conditions that may commonly be seen in to primary care: **recurrent herpes zoster (shingles), oral candidiasis (oral thrush)**, and **seborrhoeic dermatitis**.

Herpes zoster (shingles) is caused by reactivated varicella-zoster virus, the virus that also causes chickenpox. It can occur among anyone that has had chickenpox, a common childhood infection. It typically presents as a painful, localized skin rash occurring along the line of a single nerve. Among immunocompromised people, such as those with HIV, it can occur at any age, whereas in the general population it is more common among older adults. Zoster is common in individuals with HIV, particularly those with low CD4 cell counts or who have recently started treatment, and can occur before the onset of other HIV-related symptoms. It can be particularly painful in HIV-infected individuals, and complications are more common, including long-standing nerve pain, called post-herpetic neuralgia. Treatment includes antivirals such as acyclovir and valaciclovir, which may need to be administered long-term if herpes zoster is recurrent. Antiretroviral therapy may be required. Analgesia may be required to treat post herpetic neuralgia.

Oral candidiasis (oral thrush) is caused by yeast infection, found commonly in the gastrointestinal tract, regardless of HIV status. It is more common among immunocompromised individuals, and more likely to be drug-resistant, requiring more complicated treatment strategies. Up to 90% of individuals with advanced HIV infection develop oral candidiasis, with 60% having at least one episode per year, often with frequent recurrences. Depending on the degree of immunosuppression, oral candida can present as a white coated tongue, or thick white or yellowish spots on the inside of the cheeks that can be scraped off with a tongue depressor. Candida can cause inflammation leading to a red, fleshy appearance with few plaques. It can be extremely painful, making eating a challenge and further exacerbating HIV related weight loss. Extensive oral thrush should always lead to a consideration of whether the patient could be immunosuppressed. Antifungal treatment and antiretroviral therapy may be indicated.

Seborrhoeic dermatitis is a common skin condition which can indicate underlying immune suppression, especially if severe or difficult to treat, or if combined with other conditions such as shingles or oral candida. The cause of it is not clear, but it is thought to be linked to a strain of fungus that is normally found on the skin. It is one of the most common skin manifestations of HIV, and occurs in 85-95% of patients with advanced HIV infection (as compared to 3-5% of the general population). It is a dry, scaling, inflammatory skin condition that may flare and subside over time. It is characterized by itchy, reddish or pink patches of skin, accompanied by greasy flakes or scales. It most commonly occurs in the scalp and on the face, but may develop on the ears, chest, upper back, and groin. Occasionally, seborrheic dermatitis may be severe, involving large areas of the body and prove resistant to common therapies. Severe manifestations are more likely with advanced HIV infection. Antiretroviral therapy and topical treatments may be required.

HIV TESTING

12. Why is a patient's HIV status not always disclosed to their GP?

Under the common law duty of confidentiality, a medical professional is only entitled to share personal information about a patient in two situations: with the patient's consent or if the disclosure is in the public interest.

Patients are encouraged to allow for their HIV status to be disclosed to their GP or other healthcare provider in order to improve their care, and this will take place in most cases. However if a patient refuses to allow their personal information to be shared with another healthcare professional (e.g. for an aspect of their care to be referred from their HIV clinic to their GP) their wishes must be respected, unless it is considered that failure to disclose the information will put the patient, healthcare workers or other patients at risk.

Guidance on this subject is available from the General Medical Council: http://www.gmc-uk.org/Confidentiality_disclosing_info_serious_commun_diseases_2009.pdf_27493404.pdf

The National AIDS Trust released a policy report in January 2014 entitled *HIV Patient Information and NHS Confidentiality in England*, which discusses this and related issues: http://www.nat.org.uk/media/Files/Publications/Jan-2014-HIV-Patient-Confidentiality-NHS.pdf

13. How can trainers help local authorities to overcome financial barriers to the introduction of routine testing?

PHE has recently published an HIV testing evidence summary[7], which discusses the relationship between cost effectiveness of expanded HIV testing in primary care and local HIV prevalence.: http://www.hpa.org.uk/hivtesting

Expenditure on HIV care in England is around £1 billion per year, excluding the costs of tests and psychosocial care. This represents an average annual expenditure of £13,900 for each patient accessing care. Each new case of HIV infection is estimated to represent between £280,000 and £360,000 in lifetime treatment costs[8] (Health Protection Agency HIV report, 2009).

There are significantly higher costs of care for individuals diagnosed late. Direct medical costs for HIV care in the first year after diagnosis are twice as high for those diagnosed with a CD4 count less than 350 cells/mm3. This is largely due to increased inpatient hospital care costs, which are 15 times higher for those diagnosed late. The costs of HIV care remain 50% higher in the years following diagnosis, due to increased rate of hospital admission and increased costs of antiretroviral therapy[9].

Public Health England is carrying out a health economics review of the cost effectiveness of HIV testing in the UK, which will be available later this year. In the meantime the 3Cs & HIV team would be happy to deal with any specific questions about cost effectiveness.

14. What examples are available of look-back exercises for late diagnosis, and studies of missed opportunities for testing?

A collaborative project has been underway in South West England since 2011, between Public Health England, local public health teams and NHS Trusts, to classify cases of very late diagnosis of HIV as serious incidents in order to learn how to prevent them. In order to facilitate this, a root cause analysis tool and protocol has been developed for reporting cases on a monthly basis. Please contact the 3Cs & HIV team if you would like copies of these documents.

Two audits carried out by the British HIV Association (BHIVA) have looked into missed opportunities for testing in the UK. In 2008, a survey of newly diagnosed HIV positive black African individuals reported that in the 12 months preceding their diagnosis 76% had presented to health care services and 15% to inpatient services[10]. In 2012, an audit performed on behalf of the British HIV Association (BHIVA) found that there had been missed opportunities for an earlier HIV diagnosis in a quarter of newly diagnosed HIV positive individuals[11].

15. What is the existing guidance on testing for those aged over 50?

BHIVA standards of care published in 2013 do not specify an upper age limit for testing. While published rates of HIV prevalence are based on the population aged 15-59, this is not intended to mean that those aged over 59 should not be considered for testing.

In 2012, one in four adults living with diagnosed HIV were aged 50 years and over. A higher proportion of older adults, aged 50 years and over, were diagnosed late compared to adults aged under 50 (63% vs. 44%)[12]. One-year mortality is particularly marked for people aged 50 years and over at diagnosis, where more than one in 10 diagnosed late died within a year.

ONGOING SUPPORT

The 3Cs & HIV team is happy to address any specific questions you may have about HIV testing, or to discuss the HIV testing aspect of the training more generally.

The suggested point of contact for questions about HIV testing is Tom Hartney, scientist on the PHE Sexual Health Promotion team, who can be reached by email at thomas.hartney@phe.gov.uk, or by phone at 020 8327 7461.

Alternative contacts for questions about HIV testing are Samantha Westrop (samantha.Westrop@phe.gov.uk) or Anthony Nardone (anthony.Nardone@phe.gov.uk). Clinical questions should be directed to our clinical advisor, Rachael Jones (Rachael.Jones@chelwest.nhs.uk).

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