In the UK, we now live in an era of successful and accessible HIV treatment, which helps to enable normal life expectancy and good physical health. Moreover, people living with HIV who are receiving effective treatment cannot transmit the virus to sexual partners and can conceive a family without fear of vertical transmission to the foetus. However, despite advances in treatment and positive national trends for HIV care outcomes, the idea that all those infections can easily access care, take their medications, enjoy positive wellbeing and cease transmission has not become a universal reality. Many people living with HIV continue to experience a multitude of challenges that impede their ability to achieve these outcomes.

Nurses working in HIV care must have a clear understanding of the complex factors that determine good health for their patients and be able to work beyond the medical model to understand what drives poor health outcomes.

Medical management: anti-retroviral therapy

In the absence of a cure or vaccine for HIV, ensuring patients receive effective treatment remains the main goal of HIV medical management. Treatment aims to achieve an undetectable amount of virus in the blood (viral load) by using anti-retroviral drugs. An undetectable viral load means there are <40 copies of the virus per millilitre of blood – the detectable threshold for the test. The term ‘undetectable’ does not mean the person has no virus at all, and patients must be counselled on this terminology.

A sustained undetectable viral load has two benefits:
- It means CD4 cells (a type of lymphocyte – see part 1 for more details) are preserved, contributing to a healthy immune system;
- As per ‘undetectable equals untransmittable’ (U=U), people living with HIV who have a sustained undetectable viral load cannot transmit HIV to sexual partners.

Anti-retroviral drugs work by targeting and inhibiting the different phases of the HIV lifecycle, which suppresses the rate of viral replication. The HIV lifecycle was outlined in part 1 of the series and is briefly refreshed in Box 1.

HIV and drug resistance

HIV has a high speed of replication and each infected CD4 cell can produce thousands of new virions during its short...
lifespan, equating to millions of new virions being created every day (De Boer et al, 2010). Due to the speed at which HIV replicates, mistakes are often made when building the new virions; these are called mutations.

A virus without any mutations is called a ‘wild type’ and is the most dominant and ‘fittest’ in the blood. Viruses with mutations are often weaker and inferior, and are sometimes unable to replicate. Most mutations confer no advantage whatsoever, but some confer drug resistance, which could prevent an anti-retroviral drug – or even an entire class of drugs – from working.

For people not on treatment or who are undiagnosed, the wild-type virus remains the most superior and prevalent; drug-resistant mutations are inferior. For those on effective treatment, viral replication is suppressed significantly; this reduces new mutations and supresses existing drug-resistant mutations. However, inadequate treatment could allow the drug-resistant mutations to become dominant, meaning the drugs that previously controlled the individual’s HIV may no longer be effective.

To combat drug resistance, combination therapy is now the standard treatment: patients are given three or four drugs from at least two classes (Table 1). As each class targets a different stage of the HIV lifecycle, if a mutation occurs that confers resistance to one of the drugs, the other drugs in the combination will suppress reproduction of that mutation. This combination is called highly active anti-retroviral therapy (HAART).

Before a patient starts treatment, or if treatment fails, a blood test can be performed for resistance testing. This test generates a report of the mutations present and their impact on each anti-retroviral drug. The reports must be carefully interpreted in conjunction with the patient’s drug history.

Supporting adherence
Many HIV drug regimens are now available in a combined, once-daily single-dose tablet. This can help improve adherence by reducing pill burden. Researchers have correlated single-dose regimens with better virological suppression, improved patient satisfaction, reduced hospitalisation and reduced healthcare costs (Truong et al, 2015). Examples of combined, single-dose tablets include:

- Bikatarvy® – combines bictegravir, emtricitabine and tenofovir alafenamide;
- Triumeq® – combines dolutegravir, abacavir and lamivudine;
- Delstrigo® – combines doravirine, lamivudine and tenofovir disoproxil.

New ways of delivering HIV medications are also being developed, which may offer a solution to suboptimal adherence. Clinical trials are currently underway for long-acting injections, such as cabotegravir, an injectable anti-retroviral drug that patients receive once a month instead of taking daily tablets.

Key practice points
The British HIV Association’s (2016) guidelines are used to guide practice for anti-retroviral therapy and monitoring, and recommended as further reading. Below are some key points from the guidance:

- All patients with HIV should be started on anti-retroviral therapy, even if they have no symptoms or a good CD4 count;
- Patients who are treatment-naive (never having taken anti-retroviral therapy) should, typically, be commenced on regimens comprising three different fully active anti-retroviral agents;
- Support and holistic assessment from a wider group of professionals is crucial.

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**Box 1. Simplified HIV lifecycle**

- HIV attaches to and enters CD4 cells via surface receptors (such as CCR5 receptors)
- HIV converts its single-stranded genetic information (RNA) into double-stranded genetic information (DNA) using an enzyme called reverse transcriptase
- HIV integrates the DNA into the CD4 cell nucleus using an enzyme called integrase
- HIV has now hijacked the CD4 cell as a factory for creating new copies of itself; an enzyme called protease helps create new, mature virions

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**Table 1. Common anti-retroviral classes and drugs**

<table>
<thead>
<tr>
<th>HIV lifecycle stage</th>
<th>Drug class</th>
<th>Mechanism of action</th>
<th>Drug (abbreviated name)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attachment and entry</td>
<td>Fusion inhibitors</td>
<td>Work to block HIV from attaching to or entering the CD4 cell via different mechanisms, including blocking the CCR5 surface receptors used by HIV to gain entry or interfering with the fusion between the virus and the CD4 cell</td>
<td>Enfuvirtide (T20)</td>
</tr>
<tr>
<td>Reverse transcription</td>
<td>NNRTIs (often called ‘non-nukes’)</td>
<td>Inhibits the enzyme reverse transcriptase, which is central to the conversion of RNA into DNA; HIV cannot hijack the CD4 cell without this conversion</td>
<td>Tenofovir (TDF)</td>
</tr>
<tr>
<td>Integration</td>
<td>Integrase inhibitors</td>
<td>Inhibits the enzyme integrase, blocking the integration of viral DNA into the cell nucleus; HIV cannot hijack the CD4 cell without this integration</td>
<td>Raltegravir (RAL)</td>
</tr>
<tr>
<td>Replication, budding and maturation</td>
<td>Protease inhibitors</td>
<td>Inhibits the enzyme protease, which prevents the creation of mature infectious particles</td>
<td>Ritonavir (RTV)</td>
</tr>
</tbody>
</table>

CCR = C-C chemokine receptor; DNA = deoxyribonucleic acid; NNRTI = non-nucleotide reverse transcriptase inhibitor; NRTI = nucleotide reverse transcriptase inhibitor; RNA = ribonucleic acid.
to support adherence and individual treatment plans;
- Treatment interruption or ‘holidays’ are not recommended.

Holistic health
In the UK, many indicators are measured to determine health outcomes for people living with HIV. Indicators published annually by Public Health England (PHE) include the:
- Number of patients diagnosed;
- Estimated number of people living with undiagnosed HIV;
- Number of patients diagnosed late;
- Proportion of patients who started anti-retroviral therapy within three months of diagnosis;
- Number of patients achieving viral suppression;
- Number of patients retained in care.

PHE’s (2019) report demonstrates positive outcomes: 93% of people living with HIV in the UK are diagnosed, 97% of these are receiving treatment and 97% are virally suppressed. This exceeds the global target, set by the Joint United Nations Programme on HIV/AIDS (2014), of achieving “90-90-90”, and works towards the UK’s ambitious target of zero transmission by 2030.

Despite these remarkable achievements, there remain many people in the UK who are undiagnosed, living with transmittable levels of the virus, or not retained in care. Due to the recent years of financial austerity and national funding shortfalls, it also remains a challenge to maintain and extend current achievements. To close the gap and meet the 2030 target, we need to understand and engage with the hardest-to-reach populations, and work cohesively beyond the medical model to ameliorate the wider determinants of ill health.

Shaping the future of HIV services
Many factors influence the health and wellbeing of people living with HIV. Stigma, alone, remains a significant issue, which has a profound impact on wellbeing. People living with HIV can now expect a normal life expectancy; this is creating a demographic shift, whereby services need to work as part of a wider system to address the challenges of ageing with HIV and associated comorbidities.

For many people living with HIV globally, diagnosis can intersect with other circumstances that work together to adversely affect wellbeing (Fig 1). It has long been clear that we cannot treat HIV in isolation and let other problems be addressed separately; effective HIV services connect with a multitude of others, such as welfare, mental health, addiction, tuberculosis and hepatitis services. The ultimate goal is not only to achieve an undetectable viral load, but also to address biomedical, behavioural and structural influences of wellbeing.

Bayliss et al’s (2017) report highlights the need for change in HIV services, stating they must be designed to reflect the long-term nature of HIV. The report highlights the fact that services operate in a fragmented and complex care system as a challenge that will make it hard to deliver integrated HIV care in the way it will be needed in the future. The report is recommended as further reading and offers many recommendations, including:
- An increased emphasis on tailored peer support and peer navigation;
- Close partnership working with GPs, care homes and other long-term conditions services;
- The need for strong systems leadership to bring together providers and commissioners to coordinate care around the individual.

Predictors of negative outcomes
As health professionals, it is important for us to understand the broader factors that might influence wellbeing in people living with HIV, and the factors that could predict negative outcomes. Predictors of poor health have been extensively studied, but there has not always been homogeneity between different studies. A systematic review by Bulsara et al (2018) discusses some of the possible determinants (Table 2).

HIV and ageing: a new challenge for holistic wellbeing
Successful treatment means that people living with HIV are remaining healthy into older age. Although all of us have a risk of greater morbidity as we grow older, people living with HIV are more likely to develop certain age-related illnesses earlier than people who are HIV negative. Factors that influence the health trajectory of people ageing with HIV include:
- Modifiable risk factors, for example smoking;
- The long-term effects of antivirals;
- Comorbidities.

Professionals working in HIV care must, therefore, manage HIV in unison with comorbidities, polypharmacy, frailty and cognitive decline.

Renal health
Renal impairment is a leading cause of mortality and morbidity for people living with HIV. Renal function declines faster in the HIV population, with a prevalence of renal impairment of up to 38% (Ekrikpo et al, 2018), compared with 11-13% in the general population (Hill et al, 2016).

Renal impairment can often be a consequence of long-term exposure to HAART, because many of the drugs are excreted or metabolised by the kidneys. Commonly used drugs such as tenofovir disoproxil fumarate can be nephrotoxic, and other anti-retroviral inhibitors excretion of creatinine and cause a rise in serum creatinine. Renal impairment can also be caused:
- Directly by HIV, such as in HIV-associated nephropathy;
- Indirectly through other comorbidities, such as diabetes.

Cardiovascular health
The risk of having a myocardial infarction can be up to twice as high in people with HIV, even in those without major risk factors (Althoff et al, 2016). Weight gain in older people with HIV who are on HAART is well documented: visceral adipose tissue has been shown to increase by 25% after two years on HAART (McCoomsey, 2016).

Some anti-retroviral drugs have been linked with cardiovascular disease, insulin resistance, raised lipid profile and diabetes. Modifiable risk behaviours such as diet, alcohol and smoking are, therefore, relevant.

Neurocognitive health
Cognitive dysfunction can arise from severe immunodeficiency, substance misuse, depression and multimorbidity.
Microstructural brain changes are more common in people living with HIV, but also occur as part of the normal ageing process. HIV-associated neurocognitive disorder (HAND) can have a negative impact on memory, motor speed and disorder (HAND) can have a negative process. HIV-associated neurocognitive common in people living with HIV, but managing the cohort that is medically.

HIV specialist nurses who are increasingly their viral suppression and CD4 count.

The National HIV Nurses Association (2017) recommends an annual high-quality health review to enable patients to lead healthy lives and identify holistic needs, as well as aiding early detection and the prevention of comorbidities. Recommended for further reading, NHIVNA’s (2017) guidelines outline a set of practice standards for the annual review covering: • Cardiovascular health; • Bone health; • Renal health; • Sexual and reproductive health; • Mental health and psychosocial wellbeing; • Anti-retroviral therapy and non-anti-retroviral therapy management; • Preventative medicine;

Monitoring of comorbidities;

Holistic assessments for people living with HIV should always be longitudinal, as new challenges and obstacles appear or resolve across the illness trajectory. Assessments must always be treated with care; the information elicited may be sensitive or upsetting, particularly when discussing sexual partners, behaviours or health beliefs. Health professionals must always be non-judgemental and non-coercive; they must ensure that, instead of pressuring patients to disclose information, they know how to build trust and rapport over time, and can adapt their methods to deliver meaningful health messages.

References
Holmes P (2020) BHIVA Best Practice Management Session: CNS (The Brain) – I Keep Forgetting Things. Dementia, Depression, Classification and Investigations. BHIVA.
National HIV Nurses Association (2017) HIV Annual Health Review for People Living with HIV: A Good Practice Guide. NHIVNA.

Microstructural brain changes are more common in people living with HIV, but also occur as part of the normal ageing process. HIV-associated neurocognitive disorder (HAND) can have a negative impact on memory, motor speed and psychomotor function. HIV-associated chronic inflammation, the associated long-term neurotoxicity of anti-retroviral therapy, and ageing are most likely to influence the pathogenesis of HAND (Holmes, 2020).

HAND is now rare in well-controlled HIV, but other conditions – such as Alzheimer’s disease and vascular cognitive impairment – may also have a negative impact on adherence and engagement with care.

Holistic management
HIV services should be resourced with the necessary expertise to conduct comprehensive health-needs assessments for patients living with HIV. The assessment should cover the holistic spectrum of individual wellbeing, avoiding a sole focus on their viral suppression and CD4 count.

Many HIV centres in the UK consist of HIV specialist nurses who are increasingly managing the cohort that is medically.

stable. Nurses are well placed to conduct these assessments on a regular and ongoing basis, given their experience, skill and therapeutic relationship with patients. Larger HIV centres provide access to specialist pharmacists, dietitians, psychologists, functional therapists and social workers to help patients achieve wellbeing. Peer mentors, support groups and charities also provide valuable support and resources.

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