Treatment as prevention (TasP) refers to HIV prevention methods and programmes that use antiretroviral treatment (ART) to decrease the risk of HIV transmission.

When adhered to consistently, ART can reduce the HIV viral load in an individual’s blood, semen, vaginal fluid and rectal fluid to such a low level that blood tests can’t detect it. This is described as an ‘undetectable’ viral load or viral suppression. In these circumstances, as long as someone’s viral load remains undetectable, their health will not be affected by HIV and they cannot transmit HIV to others. Viral suppression can only be confirmed if a person is accessing regular treatment support, monitoring and viral load testing from a healthcare professional.

The effectiveness of ART as a prevention tool is now undisputed – and it is being used as a public
health intervention as well as a patient-specific strategy as a result.

Starting in 2011, the landmark study HPTN 052, revealed the personal and public health benefits of early treatment. The study, which involved 1,763 mixed-status couples, found early initiation of ART in the HIV-positive partner reduced cases of onward transmission to the HIV-negative partner by 96% compared to delayed treatment. Early treatment also resulted in 41% fewer adverse health events for the person living with HIV, compared to those not receiving treatment.2

Executive Director of UNAIDS, Michel Sidibé, described the results of HPTN 052 as a ‘breakthrough’ and ‘a serious game changer [that]... will drive the prevention revolution forward.’3

A number of follow-up studies have also reported significant reductions in HIV transmission through early initiation of treatment, with new infections averted as a result.4 5 6

In 2014, the PARTNER study, in which more than 1,000 couples were enrolled, found no transmissions within mixed-status couples when the viral load of the positive partner was undetectable.7 The four-year study conducted across 14 European countries, which observed mixed status couples where the viral load of the HIV-positive partner was undetectable, found zero transmissions after couples had sex 58,000 times without a condom. The study, which included both heterosexual and gay couples, provides good evidence for the effectiveness of TasP.8

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This evidence for the effectiveness of TasP has led to new World Health Organization (WHO) guidelines for a ‘test and treat’ or ‘treat all’ strategy – increasing testing and treatment coverage by initiating all people diagnosed with HIV on ART immediately, regardless of their CD4 count or viral load, which indicates the level of HIV in the body. This approach seeks to decrease community viral load (the average viral load among a certain population) and reduce the rate of new HIV infections.9

This is a key cornerstone of UNAIDS’ 90-90-90 targets to end AIDS as a major public health problem by 2030 (90% of all people living with HIV know their HIV status, 90% of all people diagnosed are on ART, 90% of all people on ART are virally suppressed).10

As of 2017, globally 75% of people living with HIV knew their status, 79% of people living with HIV were on treatment and 81% of people on treatment were virally suppressed.11

In many countries, access to treatment, and subsequent viral suppression levels, is lower among people most at risk of contracting HIV (sometimes known as ‘key populations’) such as sex workers,
people who inject drugs and men who have sex with men, compared to the general population. For these groups, accessing treatment is hampered by punitive legal environments, the stigma surrounding HIV, and fear that a diagnosis of HIV may be disclosed to others without consent.

Testing and treatment levels are lower among men compared to women in every region in the world and worst overall in West and Central Africa, the Middle East and North Africa and Eastern Europe and Central Asia.12

Test and treat strategies

In general, countries are quickly moving to change their HIV policies to come in line with the WHO test and treat recommendations.

As of 2018, 84% of low- and middle-income countries, and all of the UNAIDS Fast-Track countries, had adopted a test and treat policy. This is compared to the 40% of low- and middle-income countries that had adopted a test and treat policy by the end of 2016, the first year the guidelines were in existence. If current commitments are kept to, by the end of 2020, 92% of all low- and middle-income countries will have adopted a test and treat strategy.13

These changes have contributed to a significant increase in the number of people on ART, which increased by 4.5 million in just two years between 2015 and 2017: from 17.2 million to 21.7 million.14
One study from South Africa estimated that the implementation of universal voluntary HIV testing and immediate treatment initiation for adults over 15 years old would decrease HIV prevalence to 1% within 50 years.\textsuperscript{15}

‘Test and treat’ in KwaZulu-Natal

ANRS 12249 was the first of five large-scale randomised trials looking at the benefits of a universal test and treat for public health, rather than for the individual or their partners.

The research took place in a rural area of KwaZulu-Natal, South Africa, where three in ten people are living with HIV – the highest prevalence in the country – and examined the population impact of scaling up immediate treatment.

Despite increasing access to HIV testing and getting people who were on treatment virally
suppressed, the results revealed that those diagnosed often did not link to medical care, or took many months to do so. Just 49% of people diagnosed ultimately started treatment. This weak link in the test and treat chain limited the number of people who went on to achieve an undetectable viral load to just 42.4% of the population, reducing any possible population-level HIV prevention benefits.

Trials testing the effectiveness of TasP for the general population in high HIV prevalence settings are ongoing. The HPTN 071 study (also known as ‘PopART’) is the largest ever HIV test and treat trial and involved around 1 million people in South Africa and Zambia between 2013 and 2018.\textsuperscript{16}

Results from the study found new HIV infections were 30\% lower in communities where test and treat was introduced alongside other proven HIV prevention measures, compared to communities that received standard care. However, researchers found that treatment coverage was lower among young people (aged 29 and under) and among men. HIV treatment and prevention programmes will need to address these coverage gaps to realise the full potential of test and treat.\textsuperscript{17}

Evidence suggests that test and treat is having a significant impact on the number of people accessing HIV treatment. For example, in Uganda, a country which introduced test and treat in 2017, the number of men beginning treatment increased by 20,000 in just one year (from 60,000 in 2016 to 80,000 in 2017), while the number of women increased by 31,000 (from 107,000 to 138,000) over the same period. The gap between people being newly diagnosed with HIV and starting treatment has also significantly reduced, falling by 45\% for men and 60\% for women.\textsuperscript{18}

In relation to key populations, a 2016 study in India among men who have sex with men and people who inject drugs found a clear correlation between treatment, viral suppression and HIV incidence in large populations – although long-term follow up is needed.\textsuperscript{19}

In-depth interviews with service providers and people living with and most affected by HIV in Uganda, South Africa, Tanzania, Malawi and Zimbabwe highlight a number of factors that complicate the issue of test and treat. While praising the approach as a ‘remarkable testimony to the achievements of the HIV response’, the study highlights potential new challenges emerging around this intervention.\textsuperscript{20}

For example, people in the study expressed different levels of readiness when it came to engaging with HIV services; some were slower than others to move from contemplating treatment to starting and staying on the treatment cascade – with some not necessarily ready for treatment immediately after testing.\textsuperscript{21}

The time it took to travel to the clinic and the costs associated with this also discouraged study participants from accessing treatment, as did mistrust of healthcare providers.\textsuperscript{22}

Although much improved in the countries studied, the capacity of health services to provide universal treatment access for people living with HIV was also an issue. In addition, the study reported concerns from health workers that test and treat would signal the end of valuable practices that helped people remain engaged in treatment, such as CD4 count monitoring.\textsuperscript{23}

Limitations of treatment as prevention

While various studies show the potential preventative effect of treatment, these benefits are not
being realised more widely for a number of reasons. Stigma, discrimination and other human rights violations deter people from seeking testing and treatment and also compromise their ability to adhere to ART.

People are also failing to access testing and treatment soon after being infected, when viral load levels are high, meaning they are more likely to transmit HIV even if they then go on to access treatment.24

Effective treatment, in combination with other interventions could help further reduce transmissions. Findings from a study looking at the use of ART alongside PrEP for mixed-status heterosexual couples from Kenya and Uganda found the combination of these two tools to have a strong preventative impact for HIV.

Around 1,000 couples were involved in the trial, 65% of whom had engaged in unprotected sex during the past month. By the end of the study, four new HIV infections had occurred, compared with 83 expected without ART or PrEP. This equates to a 95% reduction.25

Concerns have also been raised about whether people who start treatment earlier will be more likely to engage in risky sexual behaviours such as having multiple or concurrent partners and engaging in condomless sex. Although the evidence on this is limited, a study conducted among people in rural South Africa found no difference in sexual risk taking between people receiving immediate treatment for HIV under the test and treat approach, and people whose treatment was linked to their CD4 count. This suggests test and treat is not associated with riskier sexual behaviours.26

Adherence is vital to the success of treatment as prevention

The success of TasP is highly dependent upon people adhering to their treatment. It is widely agreed that once treatment is initiated it should not be interrupted. Incomplete viral suppression causes the more sensitive strains of HIV to be suppressed and the resistant strains, which are harder to treat, to become dominant.27

Adherence is an issue even where treatment is widely available. In 2011, one study from the United States of America (USA) reported that 15 years after the initiation of highly active antiretroviral therapy (HAART), and four years after the introduction of combination prevention, only 19% of 1.1 million people living with HIV in the country had an undetectable viral load.28 As of 2014, the most recent data available, of the estimated 1.1 million people living with HIV in the USA, 85% were diagnosed, but less than half (49%) were virally suppressed.29

Evidence of the effectiveness of interventions to support people living with HIV to adhere to treatment suggests that community-based approaches can improve retention rates. For example, a study in Cape Town, South Africa, examined the success of community adherence clubs, consisting of between 25 and 30 people, which were led by community healthworkers and supported by nurses. The clubs met every two months for group counselling, a brief symptom screening, and distribution of pre-packed ART. Group members were allowed to send a patient-nominated treatment supporter or ‘buddy’ to collect their ART at alternating group visits.

The study found the clubs resulted in 94% of those taking part in the study adhering to treatment after a year. In addition, the adherence clubs were associated with a 67% reduction in the risk of people being lost to follow-up.30
HIV drug resistance

There are also concerns that the widespread use of antiretroviral treatment at a population level to reduce the number of new HIV infections could lead to a significant increase in levels of HIV drug resistance (HIVDR), as a result of poor adherence and treatment interruptions.31

This may be a particular issue in sub-Saharan Africa and certain low- and middle-income countries, where weak health systems, limited access to viral load testing and fewer resources for more expensive treatment regimes may undermine the benefits of a test and treat strategy. Indeed, the most rapid rise in HIVDR has occurred in Eastern and Southern Africa.32

HIVDR tends to be highest in people on first-line antiretroviral treatment who have previously taken antiretroviral drugs (ARVs). In many contexts, this equates to women who have received ARVs as part of prevention of mother-to-child transmission services and children who were born with HIV.33

Therefore, it is vital that patient and programmatic factors that can lead to HIVDR are monitored, so the potential impact of drug resistance for the response can be mitigated.34

Other examples of treatment used as prevention

ART has been used for HIV prevention in a number of ways, some of which are discussed below.

Prevention of mother-to-child transmission (PMTCT)

Treatment as prevention has been used since the mid-1990s to prevent mother-to-child transmission (PMTCT) of HIV. In 1994, research showed how zidovudine reduced the vertical transmission of HIV from pregnant women living with HIV to their babies from 25% to 8%.35

Since then, testing pregnant women and treating HIV-positive mothers with ARVs during pregnancy, delivery and breastfeeding has been found to reduce the risk of a mother transmitting HIV to her child by up to 95%.36

The implementation of ‘Option B+’ for PMTCT, whereby any pregnant or breastfeeding woman identified as HIV-positive is offered immediate ART for life, regardless of CD4 count or clinical stage, was a precursor to the test and treat strategy now being implemented globally. Evaluations of Option B+ provide valuable lessons to inform test and treat strategies, and may serve to ensure successes are replicated and failures avoided.37

Pre-exposure prophylaxis (PrEP)

Pre-exposure prophylaxis (PrEP) is a daily course of antiretrovirals that can protect HIV-negative people from HIV before potential exposure.

Studies have shown that, when PrEP is adhered to exactly as prescribed, it reduces the chances of HIV infection to near zero.38 39 As a result, like TasP, PrEP has potential population-wide benefits.

However, if not taken consistently, PrEP is much less effective and the risk of HIV infection increases substantially. It also does not provide protection against other sexually transmitted infections and bloodborne illnesses such as hepatitis C, syphilis, or gonorrhea. A condom is the only way to protect
against both HIV and other STIs. For people who inject drugs, using clean needles each and every time will prevent infection from both HIV and other bloodborne illnesses, such as hepatitis. As a result, it is important that PrEP is offered as part of a combination package of prevention initiatives based on individual circumstances.  

In 2015, the World Health Organization (WHO) released new guidelines and a policy brief recommending that PrEP should be offered as a choice to people who are at substantial risk of HIV infection. For example, those who have an HIV-positive partner, are unable to negotiate condom use, or are having repeated sex without a condom. Previously, it was only recommended for certain key affected populations such as sex workers, men who have sex with men and people who inject drugs.  

### Microbicides

Microbicides are gels or creams containing antiretroviral drugs that are applied to the vagina to help prevent HIV infection. Vaginal microbicides are relatively effective, so long as they are used consistently and correctly. One study, the CAPRISA 004 trial in South Africa, observed 39% fewer infections generally and 54% among women who were highly adherent, but its findings have not been replicated.  

The main challenge with microbicides is adherence – in other words, creating a product that women who are at high risk of HIV infection are able to use regularly and consistently. In this respect, the issues for microbicides and PrEP are comparable. In fact, a microbicide gel is essentially a different way to deliver PrEP and is sometimes referred to as ‘topical PrEP’.

In 2016, two large clinical trials — The Ring Study, which took place in South Africa and Uganda, and ASPIRE, conducted in Malawi, South Africa, Uganda and Zimbabwe — found that use of a monthly vaginal ring containing the antiretroviral drug, dapivirine, reduced rates of HIV acquisition by around one-third overall. In both studies, women aged over 21 used the ring more consistently and so more women in this age group were protected from HIV. However, there was little impact on HIV incidence in women aged 18-21 as this age group was less likely to consistently adhere to the ring.

The HOPE trial, involving around 1,300 women in Malawi, South Africa, Uganda and Zimbabwe, found a 54% reduction in HIV risk for dapivirine ring users, compared to none users. Similarly, the DREAM trial, which took place in South Africa and Uganda and involved 900 women, showed a 54% reduction in new HIV infections. These studies are the first vaginal ring studies to report above 50% efficiency. More detailed findings from both studies will be released in 2019.

Studies into rectal microbicides, which are suitable for use during anal sex, are also ongoing. In 2016, the first Phase II trial found that a rectal microbicide being used by men who have sex with men and transgender women, with a reduced glycerin formulation of tenofovir gel, was safe and effective, particularly when used around the time of sex.

### Post-exposure prophylaxis (PEP)

Post-exposure prophylaxis (PEP) is short-term course of antiretroviral treatment taken after possible exposure to HIV.

Since 1998, it has been used by healthcare workers who may have been exposed to HIV-infected
fluids. More recently, it has been used as an emergency prophylaxis for those who may have been exposed during a single event (for example sexual assault, unprotected sex or sharing drug injecting equipment).

More research is needed into the effectiveness of PEP as an HIV prevention strategy. One trial from the mid-1990s, which gave zidovudine to healthcare workers exposed to HIV, prevented transmission in 81% of cases. However, the use of zidovudine in PEP has since been replaced by tenofovir as a component of a three-drug combination.

Adhering to PEP for the prescribed amount of time is crucial for it to be effective. A 2015 study among healthcare workers in Ghana, all of whom were taking PEP for between 3 and 28 days depending on the regimen, found 77% adhered to treatment. Side effects were cited as the sole reason for not taking PEP for as long as instructed, underlining the importance of providing support to help people understand and manage side effects.

The future of treatment as prevention

Increasing uptake of HIV testing, offering treatment and linking people to care reduces population level rates of HIV transmission. As a result, treatment as prevention is changing the global response to HIV.

However, its effectiveness relies on people testing for HIV and, if positive, staying on and adhering to treatment, areas that are both beset with challenges – especially in the context of groups most vulnerable to HIV. Innovative strategies to increase the number of people testing for HIV, such as self-testing and partner-supported testing services, must be expanded. Along with strategies that increase treatment adherence, such as cash transfers. A number of studies have promoted a combination of cognitive, behavioural and mixed interventions including emotional support as a means of improving adherence.

Addressing structural barriers through a human rights approach to testing and treatment programmes, which should be driven by and engage the communities they serve, is also key to effective implementation of TasP.

The cost of viral load testing must also be addressed in order to increase access to this vital part of the treatment-as-prevention cycle. Without this, the benefits of this powerful new set of preventative tools will be lost.

While TasP requires large financial investments and poses significant implementation challenges, it is potentially a highly cost-effective approach to reducing both new HIV infections and the overall global HIV burden.

Overall, there is wide support for treatment as an HIV prevention measure, and since the publication of WHO’s 2015 guidelines, progress has been made in implementing test and treat. However, this progress has been uneven, with some regions achieving far higher viral suppression rates than others.

Despite the potential positive impact of TasP, it is widely acknowledged that treatment alone will not end the global HIV epidemic. There also needs to be a comprehensive package of prevention
methods, including HIV and sexual and reproductive health education, condom use, challenges to stigma and other barriers, and behaviour change to reduce the amount of new infections in the first place.62

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