KEY POINTS:

- Evidence has now shown that individuals on effective antiretroviral treatment (ART) with an undetectable viral load cannot transmit HIV to others.
- WHO guidelines now call for ‘test and treat’ strategies – initiating all people diagnosed with HIV on ART as soon as possible after diagnosis – as a way to decrease community viral load and reduce the rate of new HIV infections.
- Treatment as prevention (TasP) will only be effective alongside the scale up of testing programmes and ART adherence support.

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 now being used as a public health intervention, as well as a patient-specific strategy.
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+ partner reduced cases of onward transmission to the HIV- 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 until their CD4 count fell to 200-250 copies per mm$^3$.

Following the results of HPTN 052, Executive Director of UNAIDS Michel Sidibé, commented:

This breakthrough is a serious game changer and will drive the prevention revolution forward. It makes HIV treatment a new priority prevention option.

A number of follow-up studies since have also reported significant reductions in HIV transmission, with new infections averted as a result. 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. 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.

The PARTNER study (2016)

Viral suppression from ART prevents HIV transmission

This evidence for the effectiveness of TasP has led to new World Health Organization (WHO) guidelines for a 'test and treat' strategy - increasing testing and treatment coverage by initiating all people diagnosed with HIV on ART immediately regardless of their CD4 count or viral load, thereby decreasing community viral load and reducing the rate of new HIV infections.

This is a key cornerstone of UNAIDS’ 90-90-90 targets to end AIDS as a major public health threat 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).

However, as of 2015, globally only 60% of people living with HIV knew their status, only 46% of people living with HIV were on treatment and only 38% were virally suppressed.
Moreover, access to treatment, and subsequent viral suppression levels, is lower among key populations compared to the general population in many countries, with uptake 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 also lower among men compared to women and worst in West and Central Africa, the Middle East and North Africa.12

Test and treat strategies

As of 2015, of the 148 countries with information about national treatment policies or plans, approximately one-quarter had adopted a ‘test and treat’ approach, which initiates anyone testing positive for HIV on treatment regardless of their CD4 count. In addition, 44 countries had committed to adopting ‘test and treat’ by the end of 2016. Of the remaining countries reporting data to UNAIDS, 11 continue to limit ART for people who have a CD4 count of 350 cells/mm3 or lower.13

These changes have contributed to a significant increase in the number of people on ART, which rose by a third in two years (2013 to 2015), and now stands at 18.2 million people.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.15

CASE STUDY: ‘Test and treat’ in KwaZulu-Natal

A study in South Africa speculates that poor linkage to care may be the biggest obstacle to realising the population-level public health benefits of treatment as prevention.

‘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, where three in ten people are living with HIV – the highest prevalence in South Africa – and examined the population impact of scaling up treatment as prevention.

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 treatment as prevention for the general population in high HIV prevalence settings are ongoing. The HPTN 071 study, known as PopART, is currently carrying out a five-year, large-scale trial in 21 communities across South Africa and Zambia. 16

With a population size of around 1 million, it is the largest trial on universal ‘test and treat’.17

It aims to measure the costs and benefits of a combination package of interventions that includes door-to-door voluntary HIV testing using community healthcare workers and immediate treatment
for HIV-positive individuals. Preliminary results have revealed large numbers of people have taken up HIV testing via this means, and quicker linkages to care between the two rounds of the study. But so far, reaching men with HIV testing and linking young adults to care remain challenges that need to be addressed if population-level benefits of ‘test and treat’ are to be realised.

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.

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.

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.

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.

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.

**Limitations of treatment as prevention**

While the PARTNER study shows the potential preventative effect of TasP, 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.

Effective TasP 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.

**Adherence is vital to its success**

The success of treatment as prevention 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.29

Adherence is an issue even where treatment is widely available. In 2011, one study from the 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.30

A study examining the effectiveness of interventions to support people living with HIV to adhere to treatment suggests that community-based approaches can improve retention rates. The 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 health workers 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.31

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.32

This may be a particularly issue in sub-Saharan Africa and other 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.

It is therefore 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.33

Other examples of treatment used for prevention

There are other examples where ART has been used for HIV prevention:

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 HIV-infected mothers to their babies from 25% to 8%.34

Since then, testing pregnant women and treating HIV-positive mothers with antiretroviral drugs (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%.35

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.36

Evaluations of Option B+ provide valuable lessons to inform the ‘test and treat’ strategy and ensure successes are replicated and failures are avoided.37
Pre-exposure prophylaxis (PrEP)

Pre-exposure prophylaxis (PrEP) is a daily course of ARVs 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. As a result, like TasP, PrEP potentially has 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 (STIs) and blood-borne illnesses such as hepatitis C, syphilis, and gonorrhoea. (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 blood borne 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.

Studies into rectal microbicides, which are suitable for use during anal sex, are also ongoing.

Post-exposure prophylaxis (PEP)

Post-exposure prophylaxis (PEP) is short-term 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, its use in PEP has since been replaced by tenofovir as a component of a three-drug combination.

The future of treatment as prevention

Treatment as prevention has the potential to radically change the global response to HIV. Increasing uptake of HIV testing, offering treatment and linking people to care will reduce population level rates of HIV transmission.

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 the WHO’s 2015 guidelines progress has been made in implementing ‘test and treat’. This progress has however 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, stigma reduction and behaviour change to reduce the amount of new infection in the first place.

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