

Introduction

The demonstration in 2011 that HIV treatment reduces the risk of heterosexual transmission by 96% was hailed as a 'game changer' that would revolutionise HIV prevention. This briefing paper describes the scientific evidence for treatment as prevention and considers its implications for the UK. The first half of the briefing focuses on individuals and couples, before turning to possible benefits at a population level, for public health.

While antiretroviral drugs can also have prevention benefits when taken by HIV-negative people, as pre-exposure prophylaxis (PrEP) or as post-exposure prophylaxis (PEP), this briefing only covers antiretrovirals taken by people with diagnosed HIV, as treatment.

Scientific evidence

HIV treatment reduces the risk of transmission by reducing the quantity of HIV circulating in the body. When there is so little HIV in a person's blood that their viral load is 'undetectable', the risk of sexual transmission is minimal.

The HPTN 052 randomised controlled trial has conclusively demonstrated that HIV treatment significantly reduces the risk of sexual transmission. The trial recruited 1763 couples in which an HIV-positive person had a CD4 cell count between 350 and 550 cells/mm³ and had an HIV-negative partner. Almost all the couples were heterosexual and most were living in African or Asian countries.

The HIV-positive participants were randomised either to start treatment immediately, or to defer treatment until their CD4 count fell below 250 cells/mm³.

A total of 28 individuals acquired HIV from their primary partner during the trial, one in the immediate-treatment arm and 27 in the deferred-treatment arm. This amounts to 96% fewer transmissions occurring.

The single transmission in the immediate-treatment arm took place a few days either before or after the person started HIV treatment, in other words before full viral suppression had been achieved.

In considering whether HIV treatment will reduce the transmission risk by 96% in all circumstances, it is worth remembering that HPTN 052 was a clinical trial, conducted under optimum conditions – participants received

adherence and safer sex counselling as well as frequent testing for viral load and sexually transmitted infections. Moreover, the participants were couples in stable relationships in which each partner was aware of the other's HIV status; only 5% of participants reported having unprotected sex.

A large observational study (the PARTNER study) has provided preliminary data that support the findings of HPTN 052. The researchers have recruited couples in which an HIV-positive partner is taking HIV treatment and has an HIV-negative partner. In contrast to the randomised trial, all couples report using condoms inconsistently or not at all.

Importantly, approximately half of the participants are men who have sex with men. The study is being conducted in 14 European countries.

An interim analysis, with data on almost 800 couples who reported just under 45,000 acts of penetrative sex, found that there had been no transmissions from a partner with an undetectable viral load. This applies to both anal and vaginal sex.

The researchers are collecting more data, and recruiting more gay couples, so that they can provide precise estimates of the transmission risk during different sexual acts. Final results are due in 2017.

A number of smaller observational studies have been conducted with heterosexual couples only. Their results have varied somewhat, but do broadly confirm the findings of HPTN 052. These studies have consistently shown that HIV transmission occurs very infrequently when the HIV-positive partner is taking treatment or has a low viral load.

Some concerns have been raised about circumstances in which transmission could still occur, despite the person with HIV taking treatment. Transmission might occur during the first few months of a person taking treatment – studies suggest that viral load is most likely to remain consistently undetectable after six months or more of treatment. If adherence is poor (i.e. drug doses are missed or taken late), viral load may rise. Temporary rises ('blips') in the viral load in sexual fluids, caused by sexually transmitted infections or menstruation, could possibly have an impact on the risk of transmission.

Different antiretroviral drugs may have different abilities to penetrate into the male genital tract, female genital tract and rectal tissue. Studies have sometimes found that

individuals have had an undetectable viral load in blood, but not in other body fluids. Nonetheless most people who have an undetectable viral load in blood are also undetectable in their semen or vaginal fluids, as well as in their rectal mucosa and (in the case of women) vaginal mucosa.

Despite these uncertainties it remains clear that, overall, effective HIV treatment has a profound impact on infectiousness and sexual transmission. People taking HIV treatment who have an undetectable HIV viral load are much less likely to pass on HIV than people not on treatment.

Expert advice and guidelines

In 2008, Swiss clinicians issued the ‘[Swiss statement](#)’, which asserted that the risk of sexual HIV transmission is minimal as long as the person with HIV is adherent to antiretroviral therapy, is under medical supervision, has had an undetectable viral load for at least six months **and** has no other sexually transmitted infections (STIs).

In 2013, [the British HIV Association \(BHIVA\) and the Department of Health’s Expert Advisory Group on AIDS \(EAGA\)](#) stated that the HPTN 052 study showed that effective antiretroviral therapy “is as effective as consistent condom use” in limiting transmission during vaginal sex. Moreover, while there are no data for anal sex, “it is expert opinion that an extremely low risk of transmission can also be anticipated”. The authors clarified that the transmission risk during vaginal or anal intercourse will be “extremely low” as long as:

- neither partner has any STIs (regular screening is recommended); **and**
- the person with HIV has had a sustained viral load in blood below 50 copies/ml for at least six months; **and**
- viral load is checked every three to four months (i.e. more often than in standard clinical care).

Both the British and Swiss statements were written with stable partnerships in mind – when meeting casual sexual partners, it is usually impossible to know if the other person has a sexually transmitted infection as there may be no symptoms. Moreover, the British authors stress that HIV treatment cannot curb the spread of gonorrhoea, chlamydia, syphilis and other sexually transmitted infections, but condoms can do so.

Advising individuals

The scientific information described above is likely to be acted upon in different ways, depending on individual attitudes to risk and risk aversion; different views about who is responsible for preventing HIV transmission; relationship dynamics; and other personal circumstances.

On the one hand, an HIV-negative partner could put pressure on a positive partner to go on treatment before they are ready. On the other hand, an HIV-positive partner might use an undetectable viral load as a means of putting pressure on the negative partner to stop using condoms. Equally, many people living with HIV are terrified of the prospect of infecting partners and may not be willing to trust their undetectable status, even if the negative partner is ready to do so.

Some people may assume that a person taking HIV treatment has a low transmission risk, without paying attention to recent results of viral load testing and STI screening. While some people with HIV may feel that there is no need to disclose their HIV status if they have an undetectable viral load, some well-informed HIV-negative individuals may ask sexual partners not only about HIV status, but also about HIV treatment and viral load.

HIV prevention workers need to be able to help people with scenarios such as these, and to clearly communicate complex information about risks and risk reduction. Advice may need to address issues of disclosure, power imbalances in relationships, and the criminalisation of HIV transmission. Clients should be encouraged to consider the prevention of other sexually transmitted infections, not just the prevention of HIV. Both people living with HIV and their HIV-negative partners may need advice.

HIV prevention workers are already used to discussing sexual activities which have a low risk of transmission, but for which there are no reliable data (for example, oral sex), while some staff also have experience in supporting people through complex decisions (for example, in relation to ‘negotiated safety’). However, workers who are more used to delivering clear messages about condoms or who have anxieties about communicating information that appears to undermine 100% condom use may benefit from discussions with colleagues or additional training.

BHIVA's [treatment guidelines](#) recommend that healthcare professionals discuss the impact of treatment on sexual transmission with all people living with HIV. An individual who wishes to take treatment in order to protect partners from the risk of HIV infection should be able to do so, even if they have no immediate clinical need for treatment themselves.

In some other countries, guidelines recommend that treatment is started earlier than in the UK, for example at a CD4 cell count of 500 cells/mm³ or as soon as the person is ready. While some experts are convinced that earlier treatment benefits the individual's health, as well as reducing the risk of transmission, [others argue](#) that this remains unproven.

The preventive benefit of treatment is also recognised in UK guidelines for [safer sex advice](#), for [post-exposure prophylaxis](#) (so that PEP might not be recommended if the 'source partner' has an undetectable viral load), and for [sperm washing](#) (which may be unnecessary if an HIV-positive man is taking effective HIV treatment).

Treatment as prevention as a policy

A wide range of policies have been described as implementing treatment as prevention (TasP), including:

1. Efforts to increase the number of people who test for HIV and the frequency with which they do so.
2. Efforts to increase the number of people living with HIV who are retained in clinical care and who take HIV treatment according to current guidelines.
3. Changing clinical guidelines so that HIV treatment is recommended to all people with diagnosed HIV, or to people at a higher CD4 cell count than at present.
4. Changing clinical guidelines so that earlier HIV treatment is recommended to specific groups, such as people who have an HIV-negative sexual partner or men who have sex with men.
5. A voluntary approach, in which HIV-positive individuals who wish to reduce their transmission risk can start treatment earlier than would otherwise be clinically recommended.
6. Informing both HIV-negative and HIV-positive people of the preventive benefits of HIV treatment.

Current UK policies mostly focus on items 1, 5 and 6 above.

The public health impact

Since treatment has prevention benefits at the individual level, it makes sense to think it may also have prevention benefits at the population level. In other words, increasing the number of HIV-positive people on treatment could lower the total amount of virus circulating in a community (also known as community viral load) and lead to a reduction in the number of new HIV infections.

This would appear to have occurred [in San Francisco](#), where the epidemic is concentrated in men who have sex with men. Between 2004 and 2008, the number of men who had recently tested went up, rates of undiagnosed infection went down and the proportion of diagnosed men with an undetectable viral load rose from 45 to 78%. During the same period of time, annual new diagnoses fell by half.

[Similarly, in British Columbia \(Canada\) between 1996 and 2012](#), the number of people taking treatment increased eight-fold, while the number of annual diagnoses was reduced by two thirds. It's estimated that for every 1% increase in the number of individuals taking treatment with a viral load below 500 copies/ml, new HIV infections (incidence) dropped by 1%.

The greatest change has been seen in people who inject drugs (92% fewer diagnoses) and this can be partly attributed to an expansion of harm-reduction services during the same period of time – consistent with this, infections with hepatitis C have also fallen. But benefit has also been seen in men who have sex with men (22% fewer diagnoses) and this does not appear to be due to increased condom use – rates of syphilis, gonorrhoea, and chlamydia have risen during the same period of time.

[A sophisticated analysis, which took into account numerous factors that influence the risk of acquiring HIV, comes from KwaZulu-Natal, South Africa](#). During a seven-year period in which access to HIV treatment expanded rapidly but unevenly, researchers followed nearly 17,000 individuals who were initially HIV negative. The analysis took into account the prevalence of diagnosed HIV and access to HIV treatment in each person's local area.

For every 1% increase in HIV treatment coverage among people with diagnosed HIV in the local community, the risk of HIV infection decreased by 1.4%. A person living in an area in which 30 to 40% of HIV-positive people were taking treatment was 38% less likely to acquire HIV than a person living in an area in which fewer than 10% of people were on treatment.

HIV treatment as prevention

A number of community randomised trials are underway in African countries to assess the population impact of treatment as prevention policies.

However, infections and diagnoses have not fallen in gay men in the UK, or in heterosexuals infected in the UK, despite even higher levels of HIV treatment coverage and viral suppression than has been achieved in San Francisco. It is estimated that approximately 2400 gay men are newly infected each year, although around nine-in-ten men with diagnosed HIV and a CD4 count below 350 cells/mm³ are taking treatment and most of them have an undetectable viral load.

Likewise, despite the widespread use of HIV treatment in Australia and the Netherlands, these countries have not seen falls in the number of infections in men who have sex with men.

This does not mean that HIV treatment is not having any benefit at all. Mathematical modelling suggests that the rate of infections would be even higher if treatment had not been provided since 1996. But it is clear that HIV treatment is not – on its own – enough to curtail the epidemic in men who have sex with men in the UK.

This is partly because of a combination of low rates of HIV testing, high rates of partner change and inconsistent use of condoms – men who have undiagnosed HIV (especially undiagnosed acute infection) are the source of most new infections. It is also possible that sexually transmitted infections curtail the preventive benefits of treatment, or that treatment is not as effective in reducing transmission during anal intercourse as during vaginal intercourse.

The treatment cascade

Diagrams of the ‘treatment cascade’ provide a useful way of visualising problems with the implementation of ‘treatment as prevention’ in specific contexts, and of identifying reasons why HIV treatment may not have as great an impact as could be hoped.

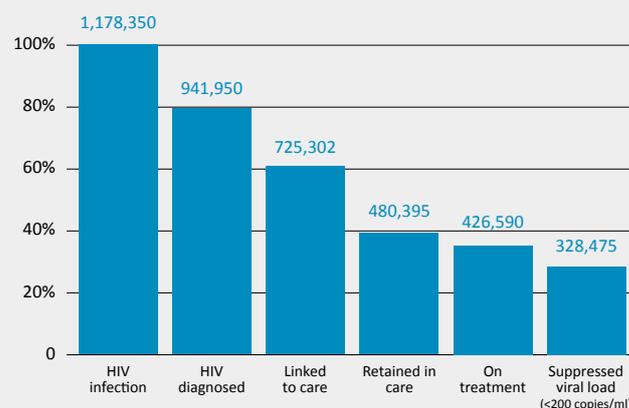
In most parts of the world, large gaps exist between the number of people who have HIV, those who know that they have HIV, those attending medical services, and those receiving effective treatment. For example, the treatment cascade for the United States shows that just 28% of those living with HIV have a suppressed viral load. This means that treatment may only have a limited impact on the

American epidemic, except in places where barriers to accessing medical care have been removed.

The equivalent diagram for the UK is more encouraging. Around 76,800 adults were living with diagnosed HIV in 2012, of whom 88% (67,600) were receiving antiretroviral treatment. Between 71% (54,800) and 78% (59,900) of adults with diagnosed HIV had an undetectable viral load (<50 copies/ml).

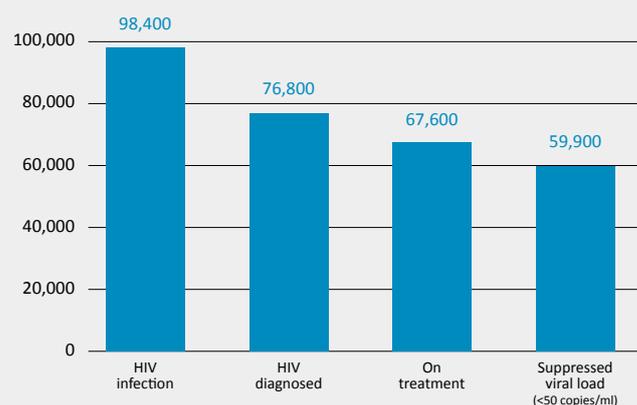
We also know that 97% of people newly diagnosed with HIV were connected with specialist care within three months, and 95% of people who attended during one year were retained in care the following year. Few other countries have comparable results.

Treatment cascade: United States, 2010



Source: Centers for Disease Control and Prevention

Treatment cascade: United Kingdom, 2012



Source: Public Health England

Furthermore, there is equality in these results, with similar figures in people of different ages, ethnicities, genders, exposure groups and geographical regions. One exception is that younger people are less likely to take treatment than older people.

But the UK has low rates of HIV testing compared to countries such as France, Australia and the United States. **In the UK, one-in-five people who have HIV are undiagnosed and half of all diagnoses are made late:** in other words, when HIV treatment is already needed (a CD4 cell count below 350 cells/mm³). Late diagnosis is especially common in heterosexual people and in older people.

As a result, only six in ten of those with HIV have an undetectable viral load. It is clear that for treatment as prevention to achieve its potential in the UK, a priority is for interventions targeting the first step in the treatment

cascade – in other words, programmes which reduce the number of people with undiagnosed HIV.

In African countries, the United States and elsewhere, health systems are often so dysfunctional that there is considerable scope to improve the numbers of people who attend medical care and receive HIV treatment. In contrast, HIV care in the UK is already of very high quality. Specifically, there are few bureaucratic or financial barriers to accessing HIV clinics in the NHS, including by people of uncertain immigration status. However, if NHS policies were changed, this could have a negative impact on engagement with care.

Moreover, while overall levels of linkage to care, retention and adherence to therapy are good, some individuals do drop out of care, attend irregularly or have problems taking their medications as prescribed. High quality, personalised support may be needed.

Finally, some individuals living with HIV may not be aware of the preventive benefits of treatment and of **BHIVA's recommendation** that any patient wishing to take HIV treatment for that reason may do so. More information for people with HIV and their partners could be provided.

Who is infectious?

In the UK, there are far more individuals with undiagnosed HIV than individuals with diagnosed HIV who are not taking antiretroviral therapy. **One analysis estimated that in 2010**, there were 14,000 HIV-positive MSM (men who have sex with men) with a viral load above 1500 copies/ml. Within this group of 'infectious' men:

- 62% (8700 men) were undiagnosed
- 5% (700 men) were on treatment which was not yet fully effective
- 16% (2300 men) were not on treatment and had a CD4 cell count above 500 cells/mm³
- 12% (1600 men) were not on treatment and had a CD4 cell count between 350 and 500 cells/mm³
- 5% (700 men) were not on treatment and had a CD4 cell count below 350 cells/mm³

Taken together, these men amount to 35% of all HIV-positive MSM in the country. The researchers examined which strategies would be most effective in reducing the size of this group. Getting *all* diagnosed men with a CD4 cell count below 500 onto treatment would reduce the proportion to 29%, while *halving* the number of undiagnosed men through increased HIV testing would reduce the proportion to 27%. It would be more effective to combine both approaches – bringing the proportion down from 35 to 21%.

Key points

- HIV treatment reduces the risk of transmission by reducing the quantity of HIV circulating in the body.
- Under specific conditions, effective treatment is likely to be as effective as condom use in limiting HIV transmission during sex.
- While the individual-level benefits of treatment as prevention are clear, there is greater uncertainty about the population-level benefits.
- Interventions to reduce the number of people with undiagnosed HIV are key to implementing treatment as prevention in the UK.
- Some HIV-prevention workers may need to develop new skills and knowledge in order to help individuals and couples understand the implications of treatment as prevention.

Further reading

Bernard EJ *Viral load and the risk of transmission*. aidsmap.com, 2013.

British HIV Association (BHIVA) and Expert Advisory Group on AIDS (EAGA) *Position statement on the use of antiretroviral therapy to reduce HIV transmission*. BHIVA/EAGA, 2013

Cohen MS et al. *Antiretroviral treatment of HIV-1 prevents transmission of HIV-1: where do we go from here?* The Lancet 382: 1515-1524, 2013.

Wilson DP *HIV Treatment as Prevention: Natural Experiments Highlight Limits of Antiretroviral Treatment as HIV Prevention*. PLoS Medicine 9(7): e1001231, 2012.

Wilton J & Broeckaert L *Treatment as prevention: do the individual prevention benefits translate to the population level?* Prevention in Focus, 2013.

Written by Roger Pebody, March 2014.

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