NHS England

Clinical Commissioning Policy: Treatment as Prevention (TasP) in HIV infected adults

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Contents

Policy Statement

NHS England will commission earlier initiation of treatment in HIV infected adults as a strategy for HIV prevention known as 'Treatment as Prevention. NHS England will commission this treatment in accordance with the criteria outlined in this document.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the population in England.

Equality Statement

Throughout the production of this document, due regard has been given to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited in under the Equality Act 2010) and those who do not share it.

Plain Language Summary

Treatment as prevention (TasP) is a term used to describe HIV prevention methods that use antiretroviral therapy (ART) treatment to significantly decrease the chance of HIV transmission between individuals, and reduce the number of new cases of HIV at population level.

In people with diagnosed HIV, the amount and activity of HIV virus in the person's bodily fluid (viral load) is the single biggest risk factor for onward transmission of HIV. Decreasing viral load not only reduces the risk of illnesses and death in the person with HIV, but also significantly decreases the risk of passing on HIV to their sexual partners. This reduced risk of onward transmission has been demonstrated in high quality studies.

In the UK, British HIV Association guidelines for HIV treatment recommend starting treatment depending on how a person's immunity is doing, which is measured with the CD4 count. The standard is to start when the CD4 count has declined to 350 cells/mm^3 or less. The guidelines also recommend as a point of good practice that clinicians discuss and offer TasP with all newly diagnosed patients whatever their CD4 count. A consistent national policy position is required to equitable access in England to TasP.

1. Introduction

To avoid preventable morbidity and mortality, people with diagnosed HIV require treatment with antiretroviral therapy (ART) when their immune system, as monitored by CD4 lymphocyte counts, shows signs of weakening. Anyone with symptomatic HIV infection should be treated urgently. Treatment as Prevention (TasP) is a prevention intervention aimed at bringing forward the time when treatment is given to people with diagnosed HIV infection in order to prevent onward transmission of HIV to sexual partners and ultimately to reduce HIV within the population.

A 'test and treat' policy for HIV infection is used in many resource rich countries including the USA and France (Gupta *et al*. 2013). Such a policy means that irrespective of CD4 count, treatment is indicated to reduce the risk of onward transmission of HIV to uninfected partners. World Health Organization (WHO) guidelines recommend that ART is initiated regardless of clinical stage or CD4 cell count when HIV-positive individuals are in a sero-discordant partnership "to reduce transmission risk" (WHO, 2013).

In the UK, treatment guidelines are produced by the British HIV Association (BHIVA) which is accredited by NICE for guideline production. These state that treatment for all patients should be initiated at a CD4 cell count of 350 cells/mm^3 or below unless a patient has cognitive impairment, renal disease or co-infection with other infections when earlier initiation is indicated, such as hepatitis B or C, or tuberculosis. They also recommend that patients wishing to start ART primarily to reduce the risk of transmission to others should be allowed to do so, at any CD4 cell count, and that this decision be taken following an assessment of the risk of transmission to sexual partners and risks and benefits to the individual of earlier treatment (Williams et al. 2012).

There is strong evidence that, among heterosexual people with HIV sero-discordant partners, there is a 96% reduction in HIV transmission from people who successfully take treatment (Cohen et al. 2011).

The best available evidence for men who have sex with men (MSM) is taken from cohort studies which show a similar reduction in transmission (Rodger et al. 2014). A large prospective cohort study of serodifferent couples sponsored by the NIHR (the PARTNER study) is ongoing and interim results indicate a very low rate (estimated rate = 0, upper 95% confidence limit 2.2 / 100 couple years) of transmission of HIV in HIV negative people when an HIV positive person is treated with antiretroviral therapy and with plasma viral load < 200 copies/mL (Rodger et al. 2014, Muessig et al. 2012). Most importantly, there were no linked transmissions (from an HIV positive partner with an undetectable viral load) after almost 44,500 sexual instances when condoms were not used, both amongst heterosexual and MSM couples.

Treatment as Prevention (TasP) has strong biological plausibility, with studies demonstrating that effective antiretroviral treatment is associated with a marked reduction in HIV virus activity in blood, semen and cervical mucosa (Muessig et al. 2012, Cambiano et al. 2014).

Economic modelling suggests that TasP is a cost effective approach and is likely to be cost saving over 15 years in men who have sex with men, due to the resulting

reductions in transmission, and given increased future use of generic drugs (Phillips et al. 2014a, 2014b). Analysis undertaken by Public Health England in developing this policy shows that 1,800 new HIV infections will be prevented. Lifetime costs per-case are estimated at between £280-360k, therefore resulting in an overall saving of between £500-647 million to the NHS (Brown, 2013).

This and further modelling data indicates that if ART is given as a prevention initiative, it will reduce the size of the overall epidemic thereby having potential for large cost savings (Keebler et al. 2014, Mackellar et al.2014, Hull et al. 2011, Murray et al. 2013, Brown et al. 2013, Mayer et al. 2013, Ambrosioni et al. 2012, Phillips 2014a, 2014b). Increasing the proportion of people who are aware of their HIV status (Department of Health, 2013), decreasing the rate and variance of partner change and increasing rate of condom use are co-dependent in achieving this overall reduction and saving and remain high priorities across the health and social care system (Phillips et al. 2013).

2. Definitions

Treatment as prevention (TasP) describes the use of ART for people with diagnosed HIV with the aim of preventing HIV transmission to others rather than primarily for their own clinical benefit.

CD4 count A measure of the strength of a person's immune system which is impacted negatively by HIV infection. A low CD4 count indicates that the patient is at risk of opportunistic infections and illness.

PEP Post-exposure prophylaxis: ART given to someone who has been exposed to HIV, to prevent them becoming infected.

PrEP Pre-exposure prophylaxis: ART given to someone who is at risk of exposure to HIV, prior to the exposure, to prevent them becoming infected.

Sero-discordant Used to describe sexual partners with different HIV status. Sometimes called 'serodifferent'.

Viral load The activity of HIV in a bodily fluid (e.g. blood, semen).

MSM Men who have sex with men.

Index case The first case of a disease, in a cohort / in an epidemiological study, as contrasted with second and subsequent cases.

3. Aim and objectives

This policy aims to:

- Reduce the risk of HIV sexual transmission and acquisition by earlier use of ART where this is deemed appropriate due to the risk of transmission and

assessment of risks and benefits to the individual.
- Reduce the number of new cases of HIV in the population.

The objectives are to:
- Provide equitable access to a proven method of HIV prevention which is cost effective and will contribute to reducing the HIV epidemic in England.

4. Epidemiology and needs assessment

HIV continues to pose a significant public health risk in England. By the end of 2012, an estimated 98,400 (CI 93,500-104,300) people were living with HIV in the UK; approximately one in five (21,900, 22% [18%- 27%]) of whom were undiagnosed and unaware of their infection (Aghaizu et al. 2013). In high risks groups including MSM, rising rates of new infections have been observed (Phillips, 2013, Fisher et al. 2007). One of the objectives of NHS England and the DH is to reduce the number of people who are unaware that they are HIV positive, both for the benefit of the individual and to reduce onward transmission, given the role that this cohort plays in continuing to drive the UK epidemic (Department of Health, 2013).

Diagnosed population in care and on treatment
In 2012, there were 76,705 adults (aged 15 years or over) receiving HIV care in the UK. Of these, 85% (6,548) received ART.

Profile of those not on treatment

Among the 11,218 patients not receiving ART in 2012, 14% (1,571) had a CD4 count <350 cells/mm^3 (and therefore should have been receiving treatment), 86% or 9,625 had a CD4 count of >350 cells/mm^3 (Brown, 2014).

Numbers starting treatment and CD4 counts

Of the 6,800 patients starting ART in 2012, 51% had CD4 count <350 cells/mm^3. The remaining 49% of patients (n=2,529) started ART with a CD4 count >350 cells/mm^3 .

Evidence from earlier treatment studies
Recent figures from the ASTRA study show that between 45-50% of people living with HIV would want to start ART at CD4 counts above 350 cells/mm^3 (45% stated this, even if it was of no benefit to their own health) (Rodger et al. 2014). Furthermore, a recent audit at Chelsea & Westminster NHS Foundation Trust's Dean Street clinic, which diagnoses a quarter of all new HIV infections in MSM in the UK, 70 out of 100 individuals requested treatment when their CD4 count was above 350 cells/mm^3 primarily to reduce the risk of transmission to others (Gazzard, 2014).

Data from the UK Seroconverters Register reports that 75% of people diagnosed during early infection are likely to start treatment within two years. This analysis is conservative for excluding people with symptomatic early infection but shows that the additional duration of TasP may only be a couple of years (Parsons et al. 2014).

Potential cohort for TasP

Public Health England has modelled changes in ART based on a continuation of treatment at CD4 <350, CD4 <500, uptake of TasP based on the ASTRA study (45%) and a 'test and treat' strategy (100% uptake of all patients diagnosed with HIV).

Given that not all patients who are already indicated to take treatment do so, assuming 100% uptake is unlikely. In addition, as the focus of the policy is about protecting sexual partners, it is important to note that not all people living with HIV are sexually active or in sero-discordant relationships and therefore will not be at increased risk of transmitting HIV infection. Finally, this policy allows access to TasP as a choice of prevention following a clinical discussion and assessment of risks and benefits, it is not mandatory. On this basis, application of 45% uptake over the 6 year period is reasonable. However, it is reasonable based on clinical advice that this impact would be gradual following implementation.

The policy would result in a change of timing of treatment for over 7,800 patients over a 6 year period. All of these patients would be eligible for ART by the end of this period based on their own disease progression.

Application of the model would also suggest that an additional 778 people living with HIV would be treated during this period as a result of this policy.

The number of eligible patients under this policy will be affected by the success of other prevention strategies such as increasing HIV testing, which may increase the numbers of patient eligible for HIV treatment in general.

Impact on public health

Public Health England estimate that 1,800 new HIV infections will be prevented as a result of this policy, impacting significantly on reducing the HIV epidemic.

Furthermore, Ecological studies have shown that scaling up of antiretroviral coverage of the population in Kwazulu Natal was associated with a reduction in population prevalence and incidence of HIV, whilst adoption of a "test and treat" approach (increasing diagnosis of HIV and offering of ART to all) has been associated with a reduction in HIV prevalence and incidence in Vancouver and San Francisco.

Extrapolation from these studies, and together with work in the UK (Phillips et al. 2014a, 2014b) would suggest that adoption of a TasP approach, as proposed in this policy, would also result in a reduction in new cases of HIV at a population level as well as between sero-discordant couples at an individual level.

5. Evidence base

Randomised Controlled Trials

The primary evidence source is a large randomised controlled trial published in the New England Journal of Medicine in which people with HIV in sero-discordant relationships were recruited to either receive immediate ART (TasP) or deferred ART after a decline in the CD4 count or the onset of HIV related symptoms (delayed therapy). The primary prevention end point was linked HIV transmission in HIV negative partners (Cohen et al. 2011). The overall risk reduction of HIV transmission resulting from early ART was 96%. There was no evidence in this study or follow up study that taking ART was associated with any increased risk behavior. Risk behavior (i.e. sex without a condom) reduced significantly in both arms of the study, likely due to extensive counselling provided. This study was open to same sex partnerships, with 18 and 19 MSM couples in the early and deferred treatment arms respectively. In this small sample, the rate of acquisition of HIV when the partner was treated with ART was zero.

Studies by risk group

A number of cohort studies have also suggested that MSM have a similar risk reduction to that seen in heterosexuals when the index case is treated with ART (Meuessig et al. 2012). The most important of these is the prospective PARTNER study which reported its results recently (Rodger et al. 2014).

Interim results from the PARTNER study reported no linked transmission during eligible follow-up (most recent viral load in the positive partner < 200 copies/mL) despite 44,500 potential exposures from sex without condoms (including 21,000 times involving anal sex). Approximately 67% of couples were heterosexual and 33% were MSM. Enrollment and follow-up is therefore continuing in MSM couples. This study also showed that ART remained protective even in the context of other sexually transmitted infections (reported in 16% of MSM couples).

This further supports the biological plausibility highlighted in the randomised controlled trial (Cohen et al. 2011), and demonstrates that the impact of ART is also significant for MSM. Available cohort studies also show a reduction in the levels of virus present in blood, semen and cervical mucosa following successful antiretroviral treatment (Muessig et al. 2012, Cambiano et al. 2014).

Efficacy compared with other prevention methods

Condoms remain a highly effective method for reducing transmission of HIV and other STI. Phillips (2013) has modelled scenarios affecting HIV infection rates. Without condom use in UK, HIV rates in MSM would have resulted in a 400% increase in incidence. However policies that rely primarily on condom use still result in high rates of new infections in the England (Phillips, 2013).

Condoms prevent contact with genital fluids by providing a physical barrier and their efficacy is reduced by factors that compromise this, for example breakage and slippage (Fidler et al. 2013, Weller et al. 2002). ART prevents HIV transmission by stopping viral replication and lowering the amount of virus within the genital compartment, making the person with HIV less infectious. Its effectiveness is dependent on good adherence to ART. Additional quality of life benefits include reduced anxiety where breakage or slippage occurs for sero-discordant couples. Protection may be reduced in the presence of other STIs (Wood et al. 2012)

although this was not seen in the PARTNER study.

There has never been a randomized controlled trial of the efficacy of condom use versus no condom use, for ethical reasons. However, several meta-analyses of observational and cohort studies of HIV infection in couples who self-reported 100% condom use have found that this strategy is about 80% (79–93%) effective in reducing HIV infections (Weller et al. 2002). The US CDC have recently reported evidence that 100% condom use has a protective benefit of 70% for anal sex compared with no condom use, and 68% compared with intermittent condom use (Smith et al. 2013). This is somewhat lower than efficacies computed for vaginal sex. However, there is a strong risk of bias in these studies as a small number of couples in which transmission occurred incorrectly reporting 100% condom use (and we know such social desirability reporting bias occurs) is enough to lead to significant under-estimation of condom efficacy.

It must be noted that it is not possible to make a direct comparison of these two strategies due to the differences in study types and outcomes considered.

Non sexual transmission

There is convincing evidence in non-sexual contexts both of the direct relationship between viral load and infectiousness, and the impact of ART on reducing viral load and thus on risk of transmission. The impact of ART in preventing mother-to-child transmission is now well established. It has been shown that mothers with HIV are much less likely to transmit HIV to their babies if their viral load is less than 1,000 copies/ ml. (Loannidis et al. 2001) Since the introduction of ART in pregnancy, less than 1% of children born to HIV positive mothers are vertically infected if appropriate interventions are taken (von Linstow et al. 2010). A retrospective, case controlled study of healthcare workers infected with HIV through needle-stick injuries, showed that higher viral loads in the source patients involved made transmission more likely (Cardo et al. 1997) Furthermore, recent guidance from Public Health England has stated that HIV positive healthcare workers who preform exposure prone procedures should decide in collaboration with their clinician "whether they wish to take antiretroviral therapy for occupational health reasons when it is not clinically indicated" (Public Health England, 2013).

a) Efficacy

People with diagnosed HIV will require ART at some point in their pathway. TasP provides an option of bringing this treatment time forward for the purpose of preventing new infections. Discussions about the benefits and risks of TasP may require additional time for discussion between patients and their clinician.

Evidence from both randomised and observational studies report that ART reduces the risk of HIV transmission by at least 96% (Cohen et al. 2011) and that this effect is actually likely to be significantly higher in the context of having an undetectable viral load.

TasP is an additional approach to HIV prevention. It is not in place of condom use and other strategies, but is an adjunct to these where one of the partners has

diagnosed HIV infection, is sexually active and has received information about the risks and benefits of taking ART.

Increasingly, TasP provides a more cost effective approach than sperm washing for those partners wishing to conceive.

b) Safety

The safety profile from currently used ART is well described. Routine monitoring and management according the BHIVA guidelines (Williams et al. 2012) supports high levels of tolerability and low levels of serious side effects. Individualised treatment and a wide choice of drugs means that most people with HIV will have access to regimens they can tolerate. These drugs are also used by HIV negative people who are potentially exposed to HIV infection through post-exposure prophylaxis (PEP).

Any decision to prescribe TasP should be based on a full discussion between clinician and patient considering the transmission risk and all the benefits and risks to the individual. Prescribing TasP would not be mandatory but a choice where required.

c) Impact on quality of life

Quality of life has not been specifically studied when treatment is used as prevention. ART can have physical and psychological side effects. People with HIV infection will require treatment when viral load increases or immunity declines. Starting treatment earlier to prevent onward transmission to partners is strongly argued by advocacy organisations to have a positive impact on psychological factors and emotional wellbeing of people with HIV (National Aids Trust, 2012).

d) Cost-effectiveness

The lifetime cost of one person acquiring HIV infection was estimated to be £280,000-£360,000 by the Health Protection Agency in 2011. Whilst this calculation is likely to reduce due to the availability of generics, it is preferable to avoid HIV infection and numerous cost effectiveness analyses have been performed to assess the impact of TasP, most of which have shown it to be cost effective or cost saving across a range of potential assumptions (Keebler et al. 2014, Phillips et al. 2014a and 2014b, Sorensen et al. 2012, Murray. 2013, Hull and Montaner. 2011).

In MSM, the latest evidence suggests that TaSP in this group is highly cost effective, with an incremental cost effectiveness ratio of <£4,000. This analysis includes modelling for the impact of increasing use of cheaper generic drugs over a 15 year period (Phillips et al. 2014b).

This policy will mean earlier rather than additional treatment costs for HIV positive people and importantly will result in significant cost avoidance of full lifetime costs of HIV infection for new HIV infections which are prevented.

The cost of drugs for treatment is one of the most critical factors in these financial models. These costs are reducing substantially as a result of introduction of generic ARV compounds and thus treatment as prevention is likely to be cost saving in the

future.

Public Health England estimates that this policy will result in additional 778 patients over a 6-year period receiving treatment than otherwise would have done so, at a cost of £75m over this period. This will result in 1,800 infections prevented, resulting in NHS savings of £14m over this period, and between £500-647m in lifetime costs to the NHS (Brown, 2014).

6. Rationale behind the policy statement

Effective ART has transformed HIV from a fatal illness to a long term, treatable condition. Whilst mortality and morbidity have reduced, focus is now on strategies to reduce new HIV transmissions . New HIV infections continue at over 6,000 per annum. New HIV infections are also considered to be a key driver of ongoing infection. Opportunities to further increase prevention strategies are key to turning the tide of the epidemic.

The effectiveness of ART has been shown in terms of improved outcomes for infected individuals and preventing infection following high risk exposure. The drugs significantly reduce the levels of HIV, including in genital fluids, to levels that make sexual transmission unlikely to occur. In 2012, it is estimated that 78% of all diagnosed patients were virally suppressed.

For people living with HIV who are sexually active and in sero-discordant relationships, earlier initiation of HIV treatment offers additional protection from the risk of HIV transmission which can continue to be present even with condom usage due to risk of condom breakage. Advocacy organisations also report the benefits of psychological well-being of people living with HIV due to reduced anxiety relating to transmission risk, further benefits to personal/sexual relationships and disclosure, and reductions in internalised stigma.

7. Criteria for commissioning

Treatment as Prevention will be routinely commissioned where all of the commissioning criteria below are met

- Laboratory confirmed diagnosis of HIV infection, and
- Sexually active, and
- Discussion between clinician and patient has identified significant risk of HIV transmission to partners without TasP, and
- Patient has considered the information relating to TasP and understands the risks and benefits and has requested TasP to prevent onward HIV transmission, and
- Regimen selected is the lowest cost, clinically appropriate option

It should be made clear to these people that the evidence for personal clinical benefit from early treatment is not yet proven, however there may be psychological benefits which derive from the ability to reduce the risk of transmission to others.

a) Exclusions

Treatment as Prevention is not routinely commissioned for

- Patients without a laboratory confirmed diagnosis of HIV
- Patients who are not sexually active deemed to be at high risk of transmitting HIV
- Patients who do not request TasP
- Patients for whom the discussion about risks and benefits of treatment is not documented
- Paediatric patients living with HIV

b) Starting and stopping criteria

The criteria for starting treatment is the assessment between clinician and patient that transmission risk to partners warrants consideration of TasP and that the patient has considered the risks and benefits to them of starting treatment.

The regimen used should follow BHIVA guidelines for using lowest cost clinically appropriate option.

Once treatment has been started it is not generally recommended to stop, unless this is clinically indicated. Although this would be subject to patient choice following discussion of risks

Changes in regimen may be required to manage individual responses to the agents used.

8. Patient pathway

HIV positive people with a CD4 count above 350 cells/mm^3 are currently routinely monitored until the CD4 count reaches a level at which treatment is indicated. Following approval of this policy, the option to start treatment would be available at higher CD4 counts in order to reduce HIV transmission. Patients not on ART are monitored every 3-4 months. Patients stable on ART are monitored every 6-12 months.

9. Governance arrangements

Management of ART is already routinely carried out in all HIV treatment centres. The monitoring of patients with other complications, including renal or liver disease or co-infection is the same for those receiving ART.

10. Mechanism for funding

NHS England is responsible for the commissioning of all antiretroviral medicines for all indications.

In 2014/15, antiretrovirals are funded as a pass through payment to commissioned Trusts.

A mandatory HIV outpatient tariff currency is currently in place which defines patients as new / new on treatment; stable; or complex. This policy would see patients as being either a) new and new on treatment in the first year or b) moving from 'stable' to 'new' (on treatment) for the year that TasP begins.

Patients with diagnosed HIV will require treatment at some point in their disease progress.

11. Audit requirements

The HIV and AIDS Reporting System (HARS) within Public Health England is the national surveillance system to monitor the HIV epidemic in the UK. Through collection of comprehensive data, PHE is able to monitor coverage of HIV treatment over time and by risk group, and describe changing HIV treatment patterns by CD4 count at ART initiation.

12. Documents which have informed this policy

(2014) 'BHIVA guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2012 (updated November 2013)

UNAIDS statement on treatment as prevention Framework

BHIVA/EAGA statement on Treatment as Prevention (Fidler, 2013)

NAT statement on Treatment as Prevention, 2013

Please see references.

13. Links to other policies

B06/PS/a Clinical commissioning policy statement: Stribild for the treatment of HIV-1 infection in adults

This policy follows the principles set out in the ethical framework that govern the commissioning of NHS healthcare and those policies dealing with the approach to

experimental treatments and processes for the management of individual funding requests (IFR).

14. Date of review

This policy will be reviewed in April 2017 unless information is received which indicates that the proposed review date should be brought forward or delayed.

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