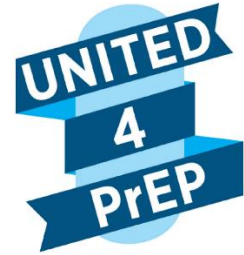


PrEP public consultation: guidance and summary



Q. What is the NHS England 45-day public consultation?

- A. The consultation is the same public consultation that was put on ice at the start of this year by NHS England. It asks for opinion on the policy specification on PrEP that was written by NHS England's Clinical Reference Group on HIV (and a sub-group specifically looking at PrEP).

The deadline to submit a response is 23 September 2016.

The full consultation, and the online survey to fill in, can be found here:

<https://www.engage.england.nhs.uk/consultation/specialised-services>

If you are responding as an individual, please don't be put off by the first page which asks for your Job Title and Organisation. You can still submit your responses and leave these (or any of the question boxes) blank.

Q. Why is it important that you respond to the consultation?

- A. A high number of positive responses, especially where they encourage improvements in the proposed policy, will add pressure on NHS England by demonstrating strong public support.

We have developed a template response to help individuals respond to the consultation.

We strongly encourage you to put in your views in support of PrEP.

It is of course entirely up to you what you write. If in what you write you are able to draw on your own experiences as an individual that will certainly add to the impact of what you say (Question 5 might be a good place to add in something from your own experience or the experience of those you know). You may well want to put things in your own words. We have in this template response put in some suggested text in response to the questions,

- which can guide you in what you write yourself,
- or which you can selectively use and build on in what you write,
- or which you can simply copy as something which reflects what you want to say.

It's up to you. **We also encourage as many organisations as possible to respond. We have developed a detailed draft response (see page 6)** which organisations (and any individuals who wish to) can read and draw on, copy or use as you see fit in putting together your own response.

Q. What do we think of the consultation document?

A. Our view overall of the consultation documents is as follows:

- We welcome the overall proposal for the commissioning of PrEP.
- The eligibility criteria for PrEP need to be clarified and strengthened for heterosexuals.
- The underlying assumptions in the cost effectiveness section of the impact assessment both underestimate the HIV transmission rate among those who would access PrEP and underestimate the effectiveness of PrEP. This means that the case for the cost-effectiveness of PrEP is unnecessarily weakened.
- Generic drugs will be available from 2018 and this will make PrEP much cheaper.
- The proposal will have far reaching and beneficial impacts on equality, though if not commissioned, the opposite would be true.
- There are concerns that the NHS England prioritisation process is not set up to prioritise prevention technologies, and that some of the particular benefits of PrEP may therefore not be recognised. This needs to be addressed.
- Some of the wider benefits of PrEP should also be brought to the attention of the NHS England panel (which the prioritisation matrix allows for). These include benefits to mental health, innovation, equalities and the wider health and social care system.

Q. Is there a summary of the documents referred to in the public consultation?

A. Yes: there are three key documents referred to in the public consultation. In addition, there are two further background documents to the consultation for information, the Clinical Panel Report and the Engagement Report where, we suggest, no comments are needed. We have summarised the three documents referred to in the public consultation briefly below:

1. **Evidence Review:** This document looks at the methodology used in compiling the evidence, the results of that evidence (both national and international studies were looked at) for different groups, and a summary of that evidence, including cost-effectiveness. It concludes that PrEP with necessary price reductions is cost-effective for an affordable public health programme of sufficient size. The cost-effectiveness

and budgetary impact of PrEP provision have been calculated for inclusion in the integrated impact assessment (below).

2. **Impact Assessment:** This document looks at the current and future patient population and demography / growth, the existing and new patient pathways, the service organisation including geography, implementation and collaborative commissioning, the cost and its impacts to both NHS England and to the NHS as a whole, the funding, financial risks, value for money and cost profile. The most pertinent of which is in the value for money section which sites the two UK cost-effectiveness analyses and concludes that PrEP may be cost-effective and cost-saving, though initially PrEP does represent a cost pressure for the NHS.
3. **Policy Proposition:** This document includes an equality statement, explains the proposed intervention bringing together the evidence base and cost-effectiveness, but it also explains about how PrEP would be commissioned, governed and audited in practice.
 - The equality statement explains that NHS England will work in line with the Equality Act 2010 and the Human Rights Act 1998.
 - The proposed intervention is around the use of antiretroviral drugs (PrEP) before exposure to HIV, given to people who don't have HIV to prevent an established infection. The groups proposed to be eligible for PrEP are:
 1. men who have sex with men, trans men and trans women: PrEP is recommended for HIV negative individuals in these groups who fulfil the criteria of:
 - having had a documented negative HIV test in the preceding year;
 - have had condomless anal intercourse in the previous 3 months;
 - are anticipated to have condomless anal intercourse in the next 3 months.
 2. serodiscordant / serodifferent couples (couples with different HIV status): PrEP is recommended for the HIV negative partner (confirmed by a documented negative HIV test in the preceding year) of a diagnosed person with HIV who is not known to be virally suppressed and where condomless sex is anticipated.
 3. heterosexual men and women: PrEP is recommended for HIV negative heterosexual people clinically assessed and known to have had condomless sex with a person with HIV (who is not known to be virally

suppressed) within the past 3 months and for whom it is anticipated that this will happen again, either with the same person or another person with similar status, and so is clinically assessed and considered to be at high risk of HIV acquisition.

- The evidence base for PrEP includes three randomised studies demonstrating effectiveness, two of which were in Europe (the UK PROUD trial and France's IPERGRAY).
- Cost-effectiveness for daily oral PrEP given to MSM in the UK have had two analyses. The first model concluded that daily PrEP use among MSM was cost-effective when targeted at MSM reporting five or more condomless sex partners in the last year, when presenting with a bacterial STI, or in men having condomless sex if the cost of antiretrovirals (for treatment and for use in PrEP) was reduced by 50% of the current British National Formulary list price. The second model looked at PrEP being offered to selected GUM clinic attendees for a one-year period compared to their life-time risk. The model suggested that PrEP is cost saving when delivered to MSM with high incidence of 5 per 100 person years, if PrEP effectiveness is at least 64%. In both analyses the period over which PrEP is cost effective and cost saving is most sensitive to the estimated HIV incidence in those eligible and to the price of antiretrovirals (ARVs).
- PrEP would be commissioned following a documented and full sexual and clinical risk assessment by a suitably qualified healthcare professional in a level 3 GU service. The eligibility criteria outlined above should be applied to establish if there is a high risk of HIV acquisition and eligibility for PrEP. The treating clinician monitors PrEP as part of an active risk reduction including health education and safer sex promotion. And the patient remains actively involved in the risk reduction intervention and is able to affirm their appropriate adherence to PrEP. This is recorded and monitored. PrEP will be stopped if the eligibility criteria is no longer met or if the person taking PrEP has confirmed HIV infection.
- The governance arrangements for PrEP would sit with Local Authorities who commission sexual health services. To ensure the quality, safety and appropriate use of PrEP:
 - access will be via named providers only;
 - all selected providers will need an agreed pathway for referral into HIV care and treatment for all patients who are tested as HIV positive, before, during or after they are prescribed PrEP;

- all selected providers will need to separately record and invoice for use of drug for PrEP.

- The funding arrangements would be that NHS England will reimburse the cost of the antiretroviral drugs used for PrEP and Local Authorities will fund the service costs associated with PrEP.
- The audit requirements for PrEP would be that all selected providers must submit individual requests for prior approval, monitor data via Public Health England surveillance systems and STI data via GUMCAD for the monitoring of impact of PrEP on STI rates.

Example response below

For organisations: example response

Please see below example responses to the key questions in the PrEP consultation. The final response must be filled in by [online form](#). As the first few questions are related to your specific organisation we have begun at question 5.

Question 5: Has all the relevant evidence been taken into account?

Yes

Comments:

Overall, the Evidence Review does take account of relevant evidence, but we mention below a few additional points.

It should be clearer in all the consultation documents that both UK models for PrEP, using conservative assumptions, found PrEP to be highly cost-effective. This makes the case for it to be commissioned from public funds. If it is not commissioned, there will be a net loss to population health.

The Evidence review also contains a recommendation for heterosexual eligibility to PrEP (at 6.2.1) which is unchanged from that of the stakeholder consultation and is at odds with the revised version as set out in the Clinical Commissioning Policy Proposition. We assume this is an oversight but we are recommending (see below) a reversion to a more flexible eligibility criterion, closer to that of the stakeholder consultation version.

Given the delays in the commissioning process for PrEP, it may be useful for a search to take place of the literature just to make sure no significant publication has emerged in the time since the analysis was last undertaken for the Evidence Review.

Question 6: Does the impact assessment fairly reflect the likely activity, budget and service impact?

No

If you have selected 'No', what is accurate?

There are a number of issues, especially in relation to the budget, to raise in relation to the impact assessment, some being additional information and others being proposed amendments.

A1.1

At the bottom of page 1 of the impact assessment where it is noted that MSM incidence is 'several times higher for MSM hence the particular focus on this population', it should also be mentioned that PHE estimate from GUMCAD data that incidence amongst black African

heterosexuals has between 2009 and 2013 been '4-5 times higher each year compared to heterosexuals overall'. See

<http://www.croiconference.org/sites/default/files/posters-2016/895.pdf>

And also:

<http://www.bashh.org/documents/Events/Conf%202015/O4%20Gwenda%20Hughes.pdf>

This is relevant to consideration of eligibility criteria for heterosexuals.

A4.2

In relation to the eligibility criteria described for PEPSE, where mention is made of high prevalence area, 'or high prevalence risk group' should be added. It might be useful in the content on PEPSE also to include some information on its cost.

C2.1

The assumptions of HIV incidence in both UK models are lower than the evidence justifies, especially as they affect estimates of cost-effectiveness and budgetary impact:

HIV incidence amongst MSM of 3.3 per 100 person-years is estimated by the PHE model, and in the UCL model it is even lower at 2 per 100 person years. The PHE model is based on MSM in 2012 who had attended a sexual health clinic for a test in the previous year and had a rectal bacterial STI. The UCL model is based on repeat testers in sexual health clinics.

These estimates are significantly lower than the incidence observed in PROUD (9%) and IPERGAY (6.6%). Experience suggests these models are conservative assumptions and actual incidence for those accessing PrEP would be significantly higher. There is for example evidence from the US that the higher the number of partners among a group of MSM, the higher proportion of men in that group are using PrEP.¹ In other words, within the group of those MSM eligible for PrEP it appears to be those at the highest risk of HIV who are most likely to access it. Such a distribution of access means that incidence will in fact be higher than in the models.

We do not see any basis for the assumption in the PHE model of a 20% increase in incidence based on risk compensation. Neither such risk compensation nor such an increase in incidence has been observed either in studies or in real world introduction of PrEP.

We also challenge the use by the PHE model of a 64% effectiveness rate. Again we see no reason for such a conservative estimate. The PROUD and IPERGAY results of 86% effectiveness seem to be a far safer basis for calculation. Other reports of the lack of new infections being diagnosed in people taking PrEP supports this, for example the Kaiser

¹ Robert M Grant et al 'Scale-up of pre-exposure prophylaxis in San Francisco to impact HIV incidence' Grant CROI Abstract 25 Seattle 2015

Permanente study in San Francisco of 388 person year of observation of PrEP use.²

C2.2

The sentence 'Generics for PrEP are expected to become available between 2018 and 2022' is in our view unduly pessimistic. The EU patent for Truvada expires in 2018. Furthermore, the Department of Health and NHS England could proactively be working to ensure a provider market is ready to supply generics competitively from 2018 once the patent expires. There are already a number of generic providers of Truvada and tenofovir/3TC fixed dose combinations in the market internationally and this fact should be noted in the impact assessment.³ We note that efavirenz and 3TC both saw reductions of 80-90% once they moved to generic provision. Therefore, the assumption of revenue cost per patient continuing to Year 6 seems again very pessimistic.

C3.1

Our reading of both PHE and UCL modeling suggests the relevant sentence should read, 'Modelling demonstrates provision of PrEP is cost effective (based on drug price and targeting access for those at highest risk of HIV, as proposed) and cost saving over a lifetime.'

C4.2

For the non-expert reader there seems to be a contradiction between the statement here that PrEP is likely to be cost saving 'after c6-10 years' and that at C3.1 where it will be 'potentially cost saving over a life time'. The text needs to clarify this apparent contradiction. It may be the difference is a result of different assumptions.

C6.1

We do not believe that the 'Availability and use of generics/drug price discounts' is a material financial risk to implementing the policy. Generic suppliers are already in the market globally and there can be no doubt that generics would be used by the NHS and patients once available. The only question is the degree of price reduction but we note HIV drugs which have recently gone generic have seen price reductions of between 80 and 90%. We strongly encourage CPAG to take a positive view of likely generic price reduction when considering the case for PrEP.

C7.1

More context is needed for the base case estimates of efficacy of 44% to 50% which were undertaken in placebo-controlled trials which has an impact on adherence and are now known not to reflect the true effectiveness.

C7.2

Again for the non-expert reader it is hard to see why here PrEP is considered a cost pressure 'for the first 20 years' whereas earlier at C3.1 it is stated that it will be a cost pressure 'most likely until Year 6'. The text needs to clarify this apparent contradiction. It may be the

² See <https://share.kaiserpermanente.org/article/large-study-of-prep-use-in-clinical-practice-shows-no-new-hiv-infections/> and also <http://www.aidsmap.com/No-new-HIV-infections-seen-in-San-Franciscos-Strut-PrEP-programme/page/3077541/>

³ See <http://www.msfacecess.org/content/untangling-web-antiretroviral-price-reductions>

difference is the result of different assumptions.

Question 7: Does the proposed policy accurately describe the groups for whom PrEP should be routinely commissioned?

No

Comments:

Since the stakeholder consultation a change has been made to eligibility criteria for heterosexuals at high risk of HIV. In the version of the Clinical Commissioning Policy Proposition which went out for stakeholder consultation the third eligibility criterion was for HIV negative heterosexual men and women 'at similar high risk of HIV acquisition' to either the HIV negative partner in a sexual relationship with an HIV positive partner who is not virally suppressed, or to MSM and trans* women at high risk of HIV acquisition (which is then defined).

In the version for public consultation, heterosexual eligibility has been changed as follows:

'HIV negative heterosexual men and women clinically assessed and known to have had condomless sex with a person with HIV (who is not known to be virally suppressed) within the past 3 months and for whom it is anticipated that this will occur again, either with the same person or another person with similar status, and so is clinically assessed and considered to be at high risk of HIV acquisition.'

We understand that this amendment has been made as a result of concerns from the PoC Board that the evidence for heterosexual risk is weaker than for MSM. The criteria were considered insufficiently specific to ensure only those at highest risk access PrEP. It also created uncertainty on the numbers who would access PrEP.

Though the commissioning concerns of the PoC Board are understandable, they must be balanced against patient need and a clinically led approach. The vast majority of HIV transmissions come from those whose HIV remains undiagnosed. Therefore, to require the partner of a heterosexual person accessing PrEP to be known to have HIV does not meet the usual risk scenario and is just a slightly altered version of criterion 2.

The criterion also does not address the significantly elevated rate of HIV incidence in the black African community and lower rates of diagnosis than for MSM.

One possible amendment would be to add the phrase 'or strongly suspected to have or to be at high risk of HIV' after the phrase 'a person with HIV (who is not known to be virally suppressed)'. This would allow for example for PrEP to be made available to a black African woman whose partner refuses to test but is known to be having sex with others. It provides the clinical flexibility needed to meet real but rare cases of high risk outside the first two criteria. We do not believe such a criterion would result in a significant number of PrEP prescriptions.

Question 8: Please provide any comments that you may have about the potential impact on equality and health inequalities which might arise as a result of the proposed changes that have been described?

Comments:

We welcome in this version of the policy the inclusion of trans* men. Given the high prevalence and incidence of HIV in black African communities we further believe that the eligibility criterion for heterosexuals must be changed along the lines we suggest or the policy will fail to meet equalities expectations and requirements. Among heterosexuals the HIV epidemic in the UK disproportionately affects women (for example, one in 22 black African heterosexual women are living with HIV compared with one in 56 black African heterosexual men⁴). The current inadequacy of the eligibility criterion for heterosexuals has a detrimental impact both on certain BAME communities and on women in particular.

HIV disproportionately affects particular groups with protected characteristics under the Equality Act 2010, in particular MSM and black African communities. The CROI poster from PHE (referred to above) uses GUMCAD data to show that whilst overall HIV incidence in 2013 amongst heterosexuals, for repeat attenders in sexual health clinics, is between 0.3 and 0.5%, incidence among black African heterosexuals is 0.19% and among MSM 1.46%. This is a substantial health inequality in relation to an extremely serious condition. Current health promotion interventions are to a degree containing the HIV epidemic but PrEP is needed if we are to see any decline in health inequalities relating to HIV.

Question 9: Are there any changes or additions you think need to be made to this document, and why?

Comments:

We are concerned, as it relates to PrEP, at the process for CPAG decision making as set out in the consultation document *'Developing a method to assist investment decisions in specialised commissioning: next steps'* April 2016, and NHS England's response dated June 2016. In para.32 of the consultation guide it states that 'the "incremental cost" of each proposal will be determined by the 'cost per patient who benefits' over five years from the drug, medical device or intervention'. This is clearly an inappropriate calculation for a preventive intervention where benefits accrue over a much longer period, indeed even, as in the case of HIV, a lifetime. It is vitally important that the prioritisation process for PrEP takes account of the differences in assessing a prevention intervention as opposed to a treatment for acute or chronic illness.

It is also the case that an innovative prevention tool such as PrEP inevitably has a greater number of variables, and thus uncertainties, than an established treatment for a known

⁴ PHE 205 'HIV in the United Kingdom – Situation Report 2015'

number of ill patients. Such uncertainty should not penalise assessment of the relative cost-benefit of PrEP.

We are conscious of the possibility of adjustment to an initial prioritisation based on consideration of four principles:

Does the drug:

- Benefit the wider health and care system?
- Advance parity between mental and physical health?
- Offer the benefit of stimulating innovation?
- Reduce health inequalities?

The case for PrEP reducing health inequalities has already been made. As a preventive intervention, there is immense potential for PrEP to benefit the wider health and care system. This is because PrEP reduces the numbers getting HIV and needing treatment and care, as well as linking those at high risk of not just HIV but other STIs into ongoing sexual health care and health promotion.

PrEP will also bring mental health benefits. Anxiety around HIV risk is a significant issue for gay men in particular. Furthermore, the prevention of HIV transmission does not only bring a physical health benefit but a mental health one also. People with HIV are about twice as likely to be diagnosed with depression as matched controls in the general population.⁵ A systematic review found that anxiety prevalence was three-times higher in HIV positive groups than among HIV negative controls.⁶

PrEP is a wholly new preventive intervention and so by definition innovative. Its introduction will, we are certain, also stimulate innovation in sexual health services and health promotion. This is because PrEP will be integrated into a combination prevention approach, as recommended by UNAIDS and WHO. PrEP will also stimulate regular testing for HIV and other STIs as recommended by both the NHS and NICE. It will help us achieve our UNAIDS 90:90:90 target by the deadline of 2020 in relation to 90% of those living with HIV being diagnosed – which is currently unmet.

We hope these considerations can be brought explicitly to the attention of CPAG in the relevant documentation.

THANK YOU

For taking the time to show your support for PrEP

⁵ Ciesla JA & Roberts JE (2001) Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry* **158**:725-730.

⁶ Clucas C et al 'A systematic review of Interventions for anxiety in people with HIV' *Psychology Health and Medicine* Vol 16 Number 5 October 2011