PrEP Impact Trial Questions and Answers

3 August 2017

1. What is HIV PrEP?

Pre-exposure prophylaxis, or PrEP, is a way for people who do not have HIV, but who are at substantial risk of HIV infection to reduce their risk of acquiring HIV. This involves taking the PrEP drug as instructed, prior to any exposures that might put the individual at high risk of getting HIV. The single-tablet PrEP drug contains two medicines (tenofovir and emtricitabine).

2. What is the PrEP Impact Trial?

The PrEP Impact Trial aims to answer key questions about the use of PrEP by groups at a higher need in England. The trial was announced by NHS England and Public Health England in a joint statement on 4th December 2016. The trial is planned to last three years and enrol 10,000 participants at high risk of acquiring HIV.

Whilst the efficacy of PrEP has been established in multiple trials across the world, including the PROUD trial that was conducted in England, the relatively small sample prevented the results being generalised to all sexually transmitted infection (STI) clinic attendees and left unanswered key questions about large-scale use of PrEP. The PrEP Impact Trial aims to address the outstanding questions about eligibility, uptake and length of use through expanding the assessment to the scale required to obtain sufficient data.

The trial is a pragmatic health technology assessment of PrEP and its implementation, that is, it aims to answer the key questions under real world conditions and at sufficient scale. In addition, the new trial will assess the impact of PrEP on new HIV diagnoses and sexually transmitted infections. The results will inform service commissioners (funders) on how to support clinical and cost effective PrEP access in the future.

3. Why is a trial needed?

A trial is necessary to address major questions that will determine effective future implementation of PrEP on a large scale. These questions are:

- What proportion of those attending sexual health clinics will be at high risk and eligible for PrEP?
- What proportion of those offered PrEP will accept it?
- What is the length of PrEP use in those who accept the offer?
- What is the impact on HIV incidence in the population?
- What is the impact on STI incidence in the population?

4. When will the trial start?

The trial aims to start in early September 2017.

5. What is meant by 10,000 participants?

The trial will enroll 10,000 participants over the next three years. It has been estimated, based on best available evidence, that this may result in around 20,000 person years on PrEP. This is because some participants may use PrEP for a very limited time, whilst others may use it continuously for three years. This is why the amount of time that PrEP is used by participants is one of the key questions to be answered by the trial.

Factors that may affect the total number of places on the trial (e.g. recruitment rate, amount of drug used, or any scientific developments) will be monitored by the trial management team throughout the lifetime of the trial. Any decision to amend the number of places would be taken by the Programme Oversight Board, which is responsible for governance of the trial.

6. Will there be enough PrEP available for those who wish to participate in the trial?

Based on planning assumptions, the trial will offer a reasonable opportunity for those assessed as meeting the eligibility criteria for the trial and willing to take it, to participate. However, it is important to remember that availability of PrEP is in the context of a clinical trial with 10,000 participants which has been designed to answer important research questions to inform future commissioning and rollout plans.

7. How will individuals be able to access PrEP in the trial?

PrEP will be offered to individuals attending participating genitourinary medicine (GUM) clinics, who meet the trial criteria and consent to participate.

8. Who will be eligible to take part in the trial, and how will participants be identified?

The trial is designed to measure how many people at high risk of acquiring HIV will take up the offer of PrEP, and so will focus on:

- men who have sex with men (MSM);
- trans men and trans women;
- HIV-negative partners of individuals diagnosed with HIV who are not known to be virally suppressed;
- heterosexual people who are considered to be at high risk of HIV acquisition.

A clinical risk assessment will be conducted at the GUM clinic.

9. What are the eligibility criteria?

The eligibility criteria for the trial are based on the criteria published by NHS England as part of the consultation on the draft commissioning policy proposal in August 2016. They were developed in discussion with clinical colleagues who participated in the Public Health England (PHE) PrEP Task and Finish Group and community representatives who participated in the Community Advisory Board convened by PHE.

PrEP will be offered to individuals considered to be at high risk of HIV acquisition. Three groups of individuals have been identified and the eligibility criteria set to match this.

a) MSM or trans women who currently test HIV negative, who also tested HIV negative earlier in the previous 12 months, and who report unprotected sex in the previous three months and consider they are likely to have unprotected sex (excluding oral sex) in the next three months.

b) The HIV negative partner of someone with diagnosed HIV, who is not known to be virally supressed and with whom unprotected sex is anticipated.

c) HIV negative people who are clinically assessed and considered to be at similar high risk of HIV acquisition as those with a partner with HIV who is not known to be virally suppressed. In other words someone who doesn't fall into the criteria set out in a or b but whose situation is assessed to be at a similar level of risk.

This means that any of the following persons may be eligible for PrEP.

1. A woman or man reporting sex without a condom with partner(s) from countries with a high prevalence of HIV and intending to continue doing so
2. A female sex worker reporting inconsistent use of condoms with clients from countries with high prevalence of HIV
3. A transgender woman who has sex with men, reporting a recent history of condomless sex and intending to continue doing so

Trial participants must be aged 16 years or over. Whilst there may be individuals under the age of 16 at high risk of acquiring HIV, the ethics of research mean that it is not possible to include these participants. Such scenarios would raise questions regarding safeguarding that would require appropriate action.

10. Will all eligible populations be able to participate in the trial?

This is a large-scale trial in order that sufficient data are generated to give certainty to commissioners to inform future commissioning of PrEP. Whilst PHE and NHS England are fairly confident that a significant proportion of those at highest risk of HIV acquisition will be eligible and enrolled, the trial has an upper limit of 10,000 participants. This means that it is possible that some eligible populations may not be able to access PrEP on the trial if it is already fully recruited.

11. Will it be 10,000 participants all followed for three years? Around 3,000 each for one year, or another scenario?

Participants will be followed for as long as they are on PrEP. No limits will be placed on enrolment into the trial annually, unless the 10,000 participant level is reached. Participant enrolment into the trial will depend on uptake of PrEP by those assessed to be eligible.

12. Where will the trial take place?

The trial will be conducted in sexual health clinics in England. All specialised genitourinary medicine (GUM) clinics (i.e. level 3 sexual health clinics) will be invited to participate in the trial. The aim is to engage as many of the 230 or so clinics as possible, both in urban and rural locations, to ensure the trial coverage is widespread and access is equitable.

Clinics participating in the trial will open to recruitment in a phased approach over a few months. It is not possible to open all sites at exactly the same time and that means that some clinics will open a few months before others. If your local clinic opens slightly later, you will still have the opportunity to join the trial. Different clinics will be ready to start at different times and the rate at which trial sites will open will be dependent on the speed at which clinics can get local approval and put systems in place to train staff and capture trial data. The PrEP Impact trial website (when available) will include a list of trial sites that are enrolling participants. This is a key area that we will continue to update on through future communications.

13. Does NHS England/PHE have an idea of the number of people they expect to recruit from each area, and how will places be allocated?

Yes, these estimates are based on best available surveillance data and will be tested during the trial. The numbers will be shared with local authorities to allow them to plan for the trial in their area.

Each trial site will initially be allocated a ring-fenced number of participants. These places on the trial are based on the current numbers of potentially eligible participants that attend GUM clinics across the UK. Recruitment will be regularly monitored by the Trial Management Group, including which population groups are being recruited. Community groups, through representation on the Community Advisory Board (CAB), Trial Management Group, and Trial Steering Committee will be kept informed of recruitment demographics and numbers.

If certain population groups at equivalent high risk of HIV are under-represented in recruitment, we will work through the CAB to encourage under-represented groups to enrol in the trial. Places will be re-allocated across sites if required to ensure equity between different HIV high-risk groups.

14. Will people from other countries in the UK (i.e. Scotland, Wales or Northern Ireland) be included in the trial?

No, the trial will only be available to people who are ordinarily resident in England. This means people who live in England and who are registered with a GP in England. People who live in Wales but are registered with an England GP would also be eligible. Those not ordinarily resident in England will not be eligible to be included in the trial.

15. Does a person's nationality or immigration status affect whether they will be able to participate in the trial?

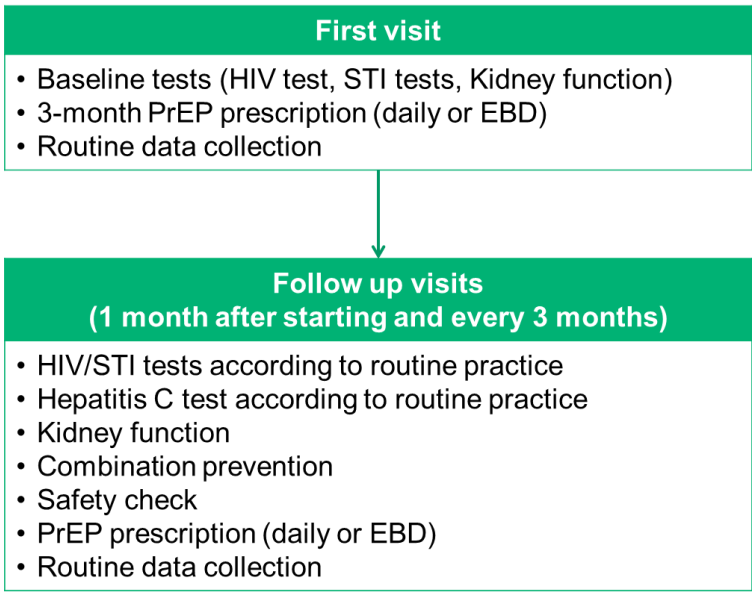
No, as long as they are ordinarily resident in England. Unlike some other NHS services, there are no immigration or nationality restrictions on accessing services provided by GUM clinics in England. This is because of the wider public health benefit of everyone being able to freely access sexual health treatment and prevention services and advice. The trial will follow the same principles.

16. What is the suggested treatment pathway for those who enrol in the trial?

The treatment pathway for participants is set out below. Clinic attendees who are part of groups at high HIV risk are expected to be individually risk-assessed when they attend. Those who are eligible for, and accept the offer of PrEP will initially be prescribed PrEP for three months, either on a daily dosing or event based regimen, depending on their risk profile. Daily dosing is when PrEP is taken on a daily basis. Event based dosing is when PrEP is taken before having sex.

For new PrEP users it is good practice to follow-up after one month to check adherence. This can be by phone, email, or in person if required. After the first month, and for existing PrEP users, participants will be advised to return to the clinic at three month intervals, in order to re-assess continued eligibility and effectiveness.

All clinical care provided to participants will be in line with clinical guidance for PrEP or established clinical practice for the off-label use of these medicines. Participants will be offered PrEP as part of an active risk reduction intervention, including health education and safer sex promotion, to reduce and modify high risk behaviour. This may include the provision of free condoms, behaviour change interventions, other biomedical interventions such as post-exposure prophylaxis where relevant, the diagnosis and treatment of sexually transmitted infections (STIs), and regular HIV testing.



17. What are the requirements for sexual health clinics to sign up as a trial site?

Trial sites will be required to meet a number of criteria to be able to participate in the trial, including:

- Adequate capacity to deliver the STI and HIV testing
- Systems in place to prescribe and dispense PrEP
- Systems in place to record and report trial data in a timely fashion

18. Who has been engaged in planning this trial and have community based organisations been involved?

The planning of the trial has been led by PHE and NHS England. The trial is overseen by the PrEP Programme Oversight Board that is jointly chaired by PHE and NHS England. The Programme Oversight Board was convened in January 2017 and now has representation from the Association of Directors of Public Health, Local Government Association, the English HIV and Sexual Health Commissioners Group (EHSHCG) and the community. There is an interim lay-representative while we recruit two new lay members to the board.

We have actively engaged with clinicians and community groups in planning the trial. There have been a series of meetings, convened by PHE, of the Task and Finish Group and Community Advisory Board. The Community Advisory Board was comprised of community representatives from across England and co-chaired by Public Health England and the National LGBT Partnership.

Membership included:

- African Health Policy Network
- National AIDS Manual
- UK Community Advisory Board (UK-CAB)

- Yorkshire MESMAC
- National AIDS Trust
- Terrence Higgins Trust
- BHA for Equality
- PrePSTER
- ClinicQ
- NAZ
- Sophia Forum
- Spectra/GMI Partnership
- Porn for PrEP UK
- African Eye Trust

The Community Advisory Board was designed to achieve participation before the trial and so has been disbanded but is being re-formed to provide advice to the Trial Management Group. The most recent meeting of the Community Advisory Board on 29 June 2017 began the transition to the PrEP Impact Trial Community Advisory Board.

The PHE PrEP Task and Finish group included representatives from the following organisations:

- British Association for Sexual Health and HIV (BASHH)
- British HIV Association (BHIVA)
- Sexual Health Commissioner from a London Local Authority
- Sexual Health Commissioner from a non-London Local Authority
- NHS England – Policy
- NHS England – Clinical
- Association of Directors of Public Health
- Local Government Association
- Public Health England Centres
- Medical Research Council
- St Stephen's AIDS Trust

The Task and Finish Group has now been disbanded. Clinical input into the trial will continue through the Trial Management Group, the independent Trial Steering Committee and the PrEP Programme Oversight Board.

19. The cost of funding 'all aspects of the trial' is put at up to £10m. Does this include the cost of the drug itself?

The £10m budget is for all aspects of the trial, including the drug.

20. Why has NHS England undertaken a competitive drug procurement for PrEP?

A formal Official Journal of the European Union (OJEU) procurement process was followed and interested parties were invited to submit applications to provide the drug. NHS England confirmed the award of a contract on 3 August 2017, in readiness for the trial to begin once ethics approval is received and trial sites are prepared.

The PrEP trial has been designed as a medicinal product assessment of emtricitabine and tenofovir disoproxil in combination which falls within an exemption in the UK Patents Act. This has allowed a competitive procurement, inviting generic suppliers and the branded manufacturer to consider participating in the trial.

21. How are clinics preparing for the trial?

St Stephen's Clinical Research and Public Health England have jointly sent out a letter to all sexual health clinics in England asking them to confirm their participation in the trial. This addresses the financial and logistical implications of participating in the trial and will allow clinics and their commissioning organisations (Local Authorities) to make the local decision as to whether they can accommodate the trial.

Once the trial team have received responses from each clinic, they will be able to send through all the relevant documents to begin the local formal approval process. Each site will need to issue an approval confirming capacity and capability before they can begin recruiting participants. As well as making sure the clinic has enough resource to run the trial, they will also need to receive trial-specific training to ensure they are appropriately trained to carry out the study tasks. The trial team will work with clinics to ensure this process is as quick as possible.

22. Has the trial received ethical approval?

The Trial has been submitted to the research Ethics Committee and is in the process of awaiting national approval. The trial team will respond quickly to any recommendations from the Research Ethics Committee and ensure that the trial is conducted to the highest ethical standards. We will continue to provide updates on the approval status of the trial in future communications.

23. How can I find out more about the PrEP trial?

For further information please email **prepimpacttrial@ststcr.com**