Pre-exposure prophylaxis to prevent HIV among MSM in the UK

The need for new prevention approaches

Nationally, one in every 17 MSM aged between 15 and 59 is living with HIV, and in London it is one in eight. There were 3,250 new HIV diagnoses in MSM in the UK in 2013, of which 2,470 were acquired in the UK. HIV incidence seems to be increasing among MSM in the UK despite expanded HIV testing services, widespread treatment of positive individuals, behaviour change interventions and provision of post-exposure prophylaxis (PEP). When used correctly and consistently condoms are a highly effective way to prevent HIV and other sexually transmitted infections. However, with HIV infections remaining high it is clear that condoms are not a sufficient option for all men. Additional HIV prevention options are urgently needed for individuals at high risk of infection (who cannot or do not always use condoms) to protect themselves, and in doing so, protect their sexual partners.

Pre-exposure prophylaxis (PrEP)

Pre-exposure prophylaxis (PrEP) is an HIV prevention strategy that involves HIV-negative individuals taking antiretroviral drugs (drugs usually used to treat HIV) to reduce their risk of becoming infected if they are exposed to the virus. The most commonly used pill for PrEP is Truvada, which combines two antiretroviral drugs.

The efficacy of Pre-exposure Prophylaxis in trial conditions

Previous placebo controlled trials of PrEP have shown efficacy ranging between 44% to 73%, although two trials among women in Africa showed no effect at all. The variations are due to differences in adherence. In placebo controlled trials, participants do not know whether they are taking the active drug, or a placebo (dummy) drug. This may lead to poor adherence, as if they believe they are likely to be on the placebo, they will not anticipate getting any benefit from taking it regularly.

On the basis of this evidence, daily Truvada was approved for HIV PrEP use in the USA in 2012, to be offered as part of a comprehensive risk reduction package usually provided by private health care schemes.

More recently, the IPERGAY study announced its results. IPERGAY was a placebo-controlled trial in France and Canada, looking at the efficacy of PrEP taken before and after sex (where two Truvada pills are taken between two to 24 hours before anticipated condomless sex, and then, if sex happened, two separate one-pill doses in the two days following sex) rather than daily dosing. IPERGAY found that PrEP was highly efficacious at preventing HIV. The only HIV infections seen were in the placebo group, or in individuals who had stopped taking their drug.

However, there were a number of important questions that needed to be addressed before clinicians

Key points

- There is an urgent need for additional HIV prevention tools, with approximately 2600 MSM being newly infected with HIV each year for the last decade.
- The PROUD study was conducted in England and showed the PrEP was highly effective at preventing HIV infection among MSM in a ‘real life’ healthcare setting.
- Taken properly, PrEP can prevent HIV infection, but it will not prevent the other sexually transmitted infections. This is why it is important to continue to promote condom use.
- HIV incidence in the population who came forward to access PrEP was much higher than we expected, based on sexual health clinic data, showing the offer of PrEP brings forward people at high risk of HIV.
- In the PROUD study PrEP use did not increase sexually transmitted infections, even though there was some evidence of a larger proportion of PrEP recipients at one year who reported receptive anal sex with 10 or more partners without a condom.
- The sexual health clinics that took part in the PROUD study were able to integrate PrEP into their routine HIV and STI risk reduction package.
and policymakers could decide if PrEP would be a feasible and cost-effective approach to tackling the HIV epidemic in the UK:

- If people know they are receiving an active drug that prevents HIV, will their risk behaviour change, offsetting the benefit of PrEP and leading PrEP to be offered to other sexually transmitted infections (STIs)?
- To whom should PrEP be offered?
- Under what conditions would PrEP be cost-effective in the UK?
- Do gay and other MSM in the UK want access to PrEP?
- Will they adhere to PrEP well enough to get prevention benefits?
- Can sexual health clinics integrate PrEP into routine practice?

PROUD

In the PROUD study 544 gay and other MSM were randomised to either receive PrEP immediately (the immediate group) or after 12 months (the deferred group). All participants were tested for HIV and other STIs approximately quarterly. This allowed researchers to compare rates of HIV and STIs between the immediate group and those who were not (in the deferred group).

- Participants were also offered the option of taking PrEP for STIs, other than HIV.
- Truvada was shown to be safe and well-tolerated in the PROUD study. This is consistent with previous studies. Side effects were infrequent, mild and transient. A small number of individuals required more frequent renal monitoring than annually, these were older participants with co-morbidities on other medications.
- While some viral resistance was seen in PROUD participants who acquired HIV, the mutations did not preclude effective treatment.
- The sexual health clinics that took part in the PROUD study were able to integrate PrEP into routine practice. Use of PrEP does not preclude effective treatment.
- Did PrEP lead to changes in risk behaviour?
- Based on self-reported sexual behaviour, there was no significant difference for either group between the number of anal sex partners at baseline and 12 months. However, there was some evidence of a larger proportion of PrEP recipients at one year who reported receptive anal sex with 10 or more partners without a condom. But self-reported data on sexual behaviour in PROUD is limited by poor levels of comprehension amongst the planned and validated sexual health clinic questionnaires and diaries. Because of this, the data on STIs is the most reliable indicator we have of whether PrEP changes sexual behaviour.

Participants in PROUD were at sufficiently high risk to show that there was interest in PrEP among some MSM, and people who presented themselves for PrEP were sufficiently at risk of HIV to benefit from PrEP. While PrEP will not be the HIV prevention method of choice for many MSM (eg. those who consistently use condoms), the results of PROUD have been enthusiastically received by community groups and participants. Groups such as NAT and the Terrence Higgins Trust have called for the NHS to make PrEP available to all who need it as soon as possible.

As part of the PROUD study we conducted in-depth one-to-one interviews with approximately 50 participants. Once analysed, these data will provide a rich understanding of how PrEP was received and how it was integrated into their everyday lives. Participants who have spoken publicly about the PROUD results have highlighted how much they appreciated the knowledge that they can avoid HIV and reduced the fear, anxiety and guilt that surrounds sex for many. Participants view PrEP as a tool to help prevent HIV during periods in people’s lives when they may take more risks than at other times in their lives. Their stories are helping people reimagine their futures without feeling that HIV is inevitable.

The conclusions of the number of new HIV infections among MSM has not decreased over the last decade. This, along with the high HIV incidence in the deferred group of PROUD, emphasises the need for PrEP in addition to current HIV prevention approaches. PrEP is highly effective at preventing HIV among MSM in the UK, in ‘real world’ conditions. Use of PrEP does not appear to increase the risk of other STIs. Providing PrEP is cost-effective or even cost-saving for the NHS, depending on who is offered it, and drug prices.
Next steps

The NHS England HIV Clinical Reference Group has appointed a sub-group to prepare the documentation for the Clinical Priorities Advisory Group to review. The review will include evaluation of clinical effectiveness, safety, cost effectiveness and affordability.

In England, the cost of the drugs used as PrEP (if commissioned) would be borne by NHS England, whose are responsible for all commissioning of antiretroviral drugs. Staff and facility costs would need to come from local authorities, who commission sexual health services. Joint commissioning will therefore be needed.

In Scotland, Wales and Northern Ireland, NHS services are commissioned and organised differently.

Recommendations

BHIVA and BASHH have reviewed the evidence and updated their position statement on PrEP, following the release of the PROUD and IPERGAY results. Their recommendations may influence clinical practice, but do not oblige commissioners to pay for it. They recommend:

- That PrEP be made available within a comprehensive HIV prevention package to MSM who are engaging in condomless anal sex, and to HIV negative partners who are in serodiscordant heterosexual and same sex relationships with a HIV positive partner whose viral replication is not suppressed.
- Healthcare workers should note that PrEP is one of several prevention tools and discuss the options available with their service users.

The PROUD researchers make the following additional recommendations:

- There are likely to be sub-populations within other risk groups (heterosexuals and injecting drug users) who would benefit from PrEP. We need research into how best to identify these individuals.
- It may be that the offer of PrEP within research projects will help to identify these sub-populations, so this research should be strongly encouraged.
- Advocates that represent these groups should direct their efforts into lobbying for funding for this research to collect the necessary evidence.

Further information

- Film about the PROUD study: https://vimeo.com/132412294
- Responses to the PROUD results http://www.proud.mrc.ac.uk/pdf/Responses%20to%20the%20PROUD%20results_24Feb2015.pdf

Contacts

For more information on the PROUD study, please email mrcctu.trial-proud@ucl.ac.uk or visit http://www.ctu.mrc.ac.uk/our_research/research_areas/hiv/studies/proud/

Credits

This briefing paper was written by Annabelle South and reviewed by the PROUD study team, Public Health England and the PROUD Community Engagement Group.

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