

Pre-exposure prophylaxis as HIV prevention in the UK

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Ther Adv Chronic Dis

2016, Vol. 7(3) 150–152

DOI: 10.1177/
2040622316647612

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Effective antiretroviral therapy has revolutionized the treatment of human immunodeficiency virus (HIV) such that mortality and morbidity rates have fallen dramatically [Public Health England, 2015]. HIV is no longer a terminal illness but a manageable long-term condition and people living with HIV, with access to effective treatment and a fully suppressed virus, can now expect a normal life expectancy and be confident they cannot pass the virus on to others.

Mathematical modelling data suggest that at least 2600 men who have sex with men (MSM) are infected with HIV every year [Public Health England, 2015]. This figure has remained the same for the last decade. This means that despite our best efforts at HIV prevention; promoting condom use, increasing HIV testing and diagnosis rates and ensuring access to effective HIV treatment, we have not been able to ‘turn the tide’ on the HIV epidemic in MSM in the UK.

Pre-exposure prophylaxis

This has led to an increasing focus on the benefits of using antiretroviral therapy more widely as a prevention strategy to protect those who are HIV negative. Pre-exposure prophylaxis (PrEP), using HIV therapy before sex that might carry a risk of HIV transmission, has been widely studied in both gay men and heterosexuals at high risk of HIV in a number of settings around the world [Baeten *et al.* 2012; Grant *et al.* 2010]. The most widely studied intervention, and the one with the best outcomes, is the use of tenofovir and emtricitabine (Truvada, Gilead, USA), a commonly used antiretroviral combination in the treatment of HIV, as PrEP. Until recently, the best data come from the USA and developing countries, but we now have really strong evidence on the efficacy and cost effectiveness of PrEP in the UK from the PROUD study. Yet, despite this, those

most at risk remain unable to access this important HIV prevention intervention here.

PROUD study

The PROUD study started recruiting in November 2012 and was designed to evaluate the impact of PrEP in a high-risk group of MSM and transgender women (TGW) in a way that reflected ‘real life’ use of the drug as closely as possible [McCormack *et al.* 2016]. There were 545 individuals who were recruited and randomly allocated to either: take Truvada straight away (the ‘immediate arm’) or to defer treatment for a year (‘the deferred arm’). Both groups then had regular 3-monthly clinic visits, completed questionnaires on sexual behaviour and adherence to the medication, and were tested for sexually transmitted infections (STIs). The deferred arm of the trial was stopped early in October 2014 because a much higher than expected incidence of HIV infections was seen in those not taking PrEP (9/100 person years rather than the expected 3/100 person years). At this point, all individuals on the deferred arm were recalled and started on PrEP.

In total, there were 20 incident HIV infections in the deferred arm and three in the group randomized to take PrEP straight away. A review of the three incident cases in the group prescribed immediate PrEP showed they were not taking PrEP at the time of infection. One was infected and seroconverted just before enrolment and the other two had failed to keep their regular study appointments and were no longer taking PrEP when infected. Overall, PrEP reduced HIV incidence by 86%. Just 13 men in a similar population would need access to 1 year of PrEP to prevent one HIV infection. Reported rates of STIs at baseline were high in both groups (which reflects the effectiveness of recruiting those most at risk of HIV) and showed no significant change

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as a result of PrEP. This reflects data from other PrEP studies which have not shown an increase in STIs in those taking PrEP. Participants continued to use condoms and other HIV risk-reduction strategies throughout the study, but not every time they had sex.

The PROUD study is not the only evidence we have for the success of PrEP in a European MSM population. The French Ipergay study, published about the same time as PROUD, was a placebo-controlled trial of event-based (or ‘on demand’) dosing [Molina *et al.* 2015]. Participants at high risk of HIV acquisition were randomized to take either placebo or active Truvada and advised to take two tablets 2–24 h before ‘risky’ sex and then to continue daily for 48 h after the last episode of sex. This study also showed an 86% reduction in HIV incidence in those taking Truvada and no difference between the two groups in rates of STIs.

Cost of PrEP

Modelling has shown that PrEP, as branded Truvada, is cost effective now if it is targeted at those at greatest risk (as measured by numbers of recent condomless sexual partners or recent STI acquisition) [Cambiano *et al.* 2015; Ong *et al.* 2015]. PrEP becomes more cost effective, and even cost saving, if the price of the drug is reduced; which would be achieved if on-demand dosing were used or when the tenofovir component of the drug comes off patent in 2017. Lifetime treatment costs for someone living with HIV are estimated to be around £360,000 and the NHS spends over £500 million a year on treatment. Although, at current prices, 1 year of Truvada costs between £3000 and £4000, PrEP is not a lifetime treatment: it is a highly effective HIV prevention tool that will protect those for whom consistent condom use is not a reality during times in their lives when HIV risks are greater. It has been estimated that, even with relatively conservative coverage in those MSM most at risk in the UK, PrEP when used in combination with increased HIV testing and HIV treatment as prevention could prevent 7400 new infections between now and 2020 [Punyacharoensin *et al.* 2016].

Truvada was licensed for use as PrEP in the USA as long ago as 2012 and there is already evidence from early roll-out programmes of the impact it is having on reducing HIV incidence when used in a combination approach to HIV prevention together with other interventions such as regular HIV

testing, promotion of condom use and treatment as prevention [Koester and Grant, 2015; Volk *et al.* 2015]. In addition to the USA, PrEP has also been made available in France, Canada, Kenya, South Africa and Israel; so why not in the UK?

PrEP availability in the UK

When the impressive results of the PROUD study were first known in the autumn of 2014, a process of applying to NHS England for approval to make PrEP available was initiated. Academics, clinicians, health economists, community organizations and patient representatives have spent the last 18 months working hard to produce the evidence and data required to support the NHS England decision-making process. Then, on 21 March 2016, at what felt very much like the ‘11th hour’ and despite all these efforts, NHS England announced its decision not to continue the process as it is not ‘responsible for commissioning HIV prevention services’ and instead offered £2 million over 2 years for pilots in selected ‘test sites’ to provide PrEP for just 500 men [NHS England, 2016]. NHS England and Public Health England planned to launch a process to seek expressions of interest from local authorities in being one of the test sites.

To say this decision was met with anger, frustration and incredulity would be an understatement. Clinicians, local authorities, directors of public health, politicians, activists and community organizations have all united in calling for NHS England to reconsider or, at least, to find an alternative process for funding PrEP. Following these calls, in a promising step forward in the campaign, NHS England have now said they will carefully consider its position on commissioning PrEP, but the sector must maintain pressure to ensure PrEP is made available as soon as possible.

Enabling access to just 500 men would be derisory, have little impact on the HIV epidemic and would only perpetuate existing inequity of access to what has been clearly shown to be a highly effective HIV prevention tool. If this plan for limited access were to go ahead clinicians would have to provide PrEP on a ‘first come, first served’ basis and would very quickly find themselves having to deny access to PrEP to men who we know are at very high risk of HIV acquisition. PrEP is undoubtedly an essential addition to our approach to combination HIV prevention and needs to be available now.

Providing PrEP to those most at risk and using it in combination with other prevention strategies would nearly halve the number of expected new infections in just the next 5 years [Punyacharoensin *et al.*, 2016]. Eight MSM are infected with HIV every day. This is entirely preventable and will continue until policy makers and commissioners start making evidence-based decisions and commit to investing in HIV prevention strategies that we know are both clinically and cost effective. We have delayed implementing PrEP in the UK for too long and to continue to deny access to those who most need it will result in unnecessary HIV infections and avoidable costs to the NHS of lifetime HIV treatment and care.

Acknowledgements

We are grateful to Victoria Bishop-Rowe (THT) for help with review and editing.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The author is also a Consultant in HIV and Sexual Health at Kings College Hospital, London and is the Principal Investigator for the PROUD study at this site.

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