

## Debate & Analysis

# HIV pre-exposure prophylaxis:

the primary care implications of prescribing restrictions

With a recent (2/8/16) high-profile court ruling backing funding for pre-exposure prophylaxis (PrEP) for HIV prevention, what is PrEP, why is it so controversial, and why should every clinician be advocating for this blockbuster drug?

### HIV IN THE UK IN 2017

The public health impact of HIV in the UK is immense. Record numbers of people are now living with the virus and over 4000 new cases are identified each year.<sup>1</sup> With recent studies estimating lifetime treatment costs to be over £360 000 per person, each new HIV diagnosis only adds further to this already immense, yet preventable, burden in our over-stretched health system.<sup>2</sup>

Men who have sex with men (MSM) are at the highest risk for HIV acquisition in the UK. Of the 4155 new diagnoses, over 81% were MSM, translating to a staggering 1 in every 20 MSM males aged 15–44 years having HIV, rising even further to 1 in every 11 in London.<sup>1</sup>

Although Public Health England (PHE) has invested significantly to curtail this epidemic, we are still seeing a rise in both incidence numbers and rates year on year. Why is this, and can more be done? Could PrEP be the magic bullet at our fingertips?

### WHAT IS PrEP?

PrEP is a novel way of using antiretroviral medication (ARV) in people who are HIV negative to avoid contracting HIV. Multiple studies have confirmed its efficacy in reducing HIV acquisition in MSM,<sup>3</sup> heterosexual couples (where one partner is HIV positive),<sup>4</sup> and in people who inject drugs (PWID),<sup>5</sup> all of whom are high-risk patients we encounter in our daily practices.

It was in 2015 that the UK-based Pragmatic Open-Label Randomised Trial of Pre-exposure Prophylaxis (PROUD) study gave a platform to PrEP by showing how it would work within the UK and the NHS. The study showed a staggering 86% reduction in HIV incidence when on PrEP as well as finding the number needed to treat with PrEP to avoid one HIV infection was only 13.<sup>6</sup>

Although this study's results mirrored other international research in the US and beyond, PROUD specifically showed how PrEP could easily be used to specifically benefit UK-based patients.<sup>7</sup> This finding is astonishing when, more than 18 months after data were published, PrEP is yet to be approved in the UK.

### WORLDWIDE UPTAKE OF PrEP

Worldwide, the reception to PrEP has been overwhelmingly positive. International bodies such as the World Health Organization (WHO) and UNAIDS now advocate its use as a core and essential part of HIV prevention strategies. A recent *Lancet* study has even suggested that PrEP could be the most powerful intervention to prevent HIV, independent from every other measure we use.<sup>8</sup> The US has over 25 000 individuals now taking PrEP since approval in 2012,<sup>9</sup> while in France it's been available since January 2016 with good uptake rates.<sup>10</sup> Several other countries in South America and Asia are also preparing to license this medication for use over the next 12 months (Figure 1).

### CONTROVERSY SURROUNDING PrEP

Despite a garrison of study evidence supporting PrEP, as well as international community approval, here in the UK scepticism towards PrEP is still rife. What are these myths and do they have a grain of truth?

#### 'PrEP will increase risky sexual behaviour'

Repeated studies show that PrEP does not increase risky sexual behaviours or undermine other safe sexual practices, such as condom use. The landmark PROUD study showed that MSM were no more likely to develop other bacterial sexually transmitted infections (STIs) (an ideal marker for risky sexual behaviour) when on PrEP. Reported condom use when on PrEP compared with when not was also equal.<sup>6</sup> Similar results

have even been shown in heterosexual couples.<sup>4</sup>

#### 'There are many drug side effects'

Although some people may experience short-term nausea and headaches after starting treatment, many large studies have shown no serious toxicity from the medication. Furthermore, and really quite essential in both the high-risk MSM and PWID groups, PrEP does not interact with alcohol or other drugs including methadone and buprenorphine, nor does it alter the effectiveness of the oral contraceptive pill.

#### 'HIV resistance will develop'

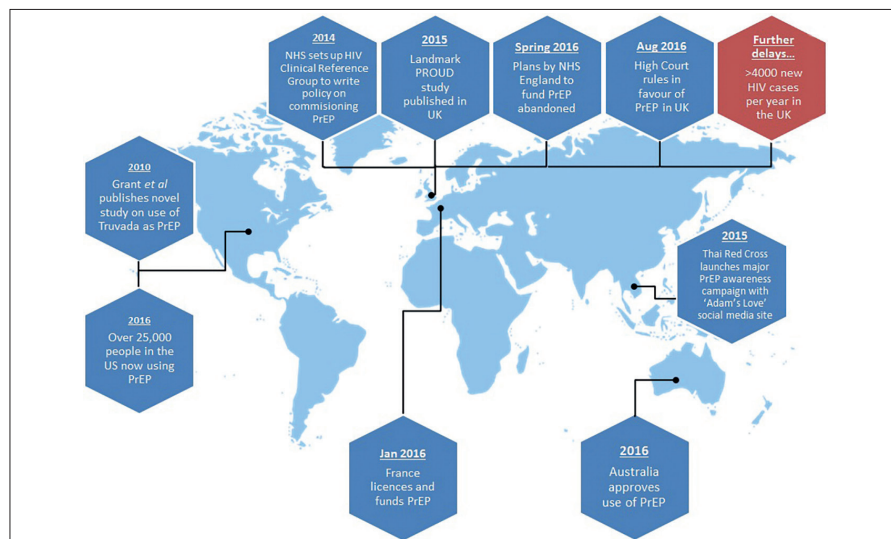
Concerns have been raised that resistance could develop in people taking PrEP if breakthrough infections occurred. Although some data do suggest that resistance could develop if PrEP was started during the period between acquiring HIV and detectable virus (seroconversion), a rational approach must be taken.<sup>11</sup> For example, the 2015 Partners PrEP Study found that, for every drug-resistant infection caused, 25 new HIV infections were prevented in the first place.<sup>11</sup>

Furthermore, with WHO guidelines advocating routine HIV testing not only before starting PrEP but also every 3 months, such resistant infections should be minimised.

#### 'PrEP is not cost-effective'

Cost-effectiveness drives the 21st-century NHS. Indeed it is expenditure that lies at the heart of the controversial delays for PrEP

Figure 1. Timeline of PrEP around the world.



approval in the UK. Despite much argument to the contrary, evidence-based data have shown that, for those at highest risk of infection, generic PrEP reduces both immediate and long-term costs to the NHS.<sup>12</sup> Currently, lifetime HIV treatment costs over £360 000 per person, but for only £43 per month a person can buy generic PrEP from abroad.<sup>2,13</sup> With UK patent expiration in 2017, similar affordable generic versions should soon be available to our own patients.

### NHS AND THE PrEP SAGA

So the evidence is clear — PrEP works. Even NHS England and PHE have backed its use. So why, if we all agree, are we not seeing our at-risk patients being protected from HIV here in the UK? In essence, cost and responsibility distribution are the issues.

Beginning in spring 2016, NHS England manipulated a legislative loophole in the Local Authority Regulations Act, stating that local authorities, not the NHS, were responsible for the 'commissioning of HIV prevention services'. The National Aids Trust, like many others, argued that this stance was bizarre and frankly incongruent when the NHS actually does fund HIV prevention measures (post-exposure prophylaxis and mother-to-child transmission, for example).

It was not until a High Court ruling in August 2016 year that the tables were turned in favour of PrEP again. The ruling by Mr Justice Green argued that NHS bosses 'had erred in deciding' it was not their responsibility and 'commissioning of PrEP is within the power of NHS England' under current legislation already.

NHS England subsequently appealed against this ruling, followed by the announcement that they would indeed fund PrEP but irritatingly only in 'trial settings'.

While further data are amassed, sorted, analysed, reported, published, and criticised further, we are forced to sit and simply allow vulnerable patients to face unnecessary harm.

### IMPLICATIONS FOR GPs

GPs are the true bastions of public health, acting as the mortar between government targets, scientific research, everyday clinical practice, and patient needs. Free condoms, routine STI checks, hepatitis A vaccinations, and counselling are already part of our comprehensive HIV prevention strategies in primary care. As knowledge of PrEP becomes more widespread, however, where does this leave GPs?

For patients who are requesting PrEP, it is not licensed for prevention outside clinical trials and so cannot be prescribed on the

NHS. For those who can afford it, however, private clinics are offering treatment for £400/month, which is most likely out of reach for our most vulnerable patients, who would reap the most benefit from this medication.

Second, many people in the UK are already buying PrEP online and multiple campaign group websites have dedicated support pages to sourcing it legally from outside the UK. For those patients who are already buying online, do we have a responsibility for monitoring them?

From a solely medical view, guidelines from the US suggest these patients require an HIV test prior to commencing PrEP and quarterly follow-up. Aside from this, however, we should also be aware of the psychological issues associated with PrEP, with much higher rates of HIV breakthrough infections reported in MSM aged 18–22.<sup>13</sup>

Although more research is clearly required on PrEP prescribing and monitoring, as well as comprehensive guidelines for primary care, what are we expected to do in the meantime for these young, sexually active men who have online access to PrEP? We cannot continue to bury our heads in the sand.

### CONCLUSION

A shift to online dating apps has moved the once more restricted onto the open internet. The combination of this with increasing rates of HIV brings a wave of new risks, and sadly, new HIV infections. As clinicians we must be able to keep pace with this and not engulf ourselves in a mountain of more data.

PrEP forms only one part of our defence. Nobody is suggesting anything else. Shown to be both a cost-effective and powerful drug, it could be the strongest single intervention that we use to stop the spread of HIV in the UK.

For a virus first identified just over 32 years ago we have made huge scientific advancements in both detection and treatment, saving thousands of lives in the process. Until now the last hurdle was prevention. Let us not fall behind the rest of the world in controlling the spread of this devastating virus. The roll-out of PrEP across the UK will go a long way in achieving control of HIV. Further delays will only cost lives.

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