Proposed Title:
The use of antiretrovirals to prevent transmission and acquisition of HIV.

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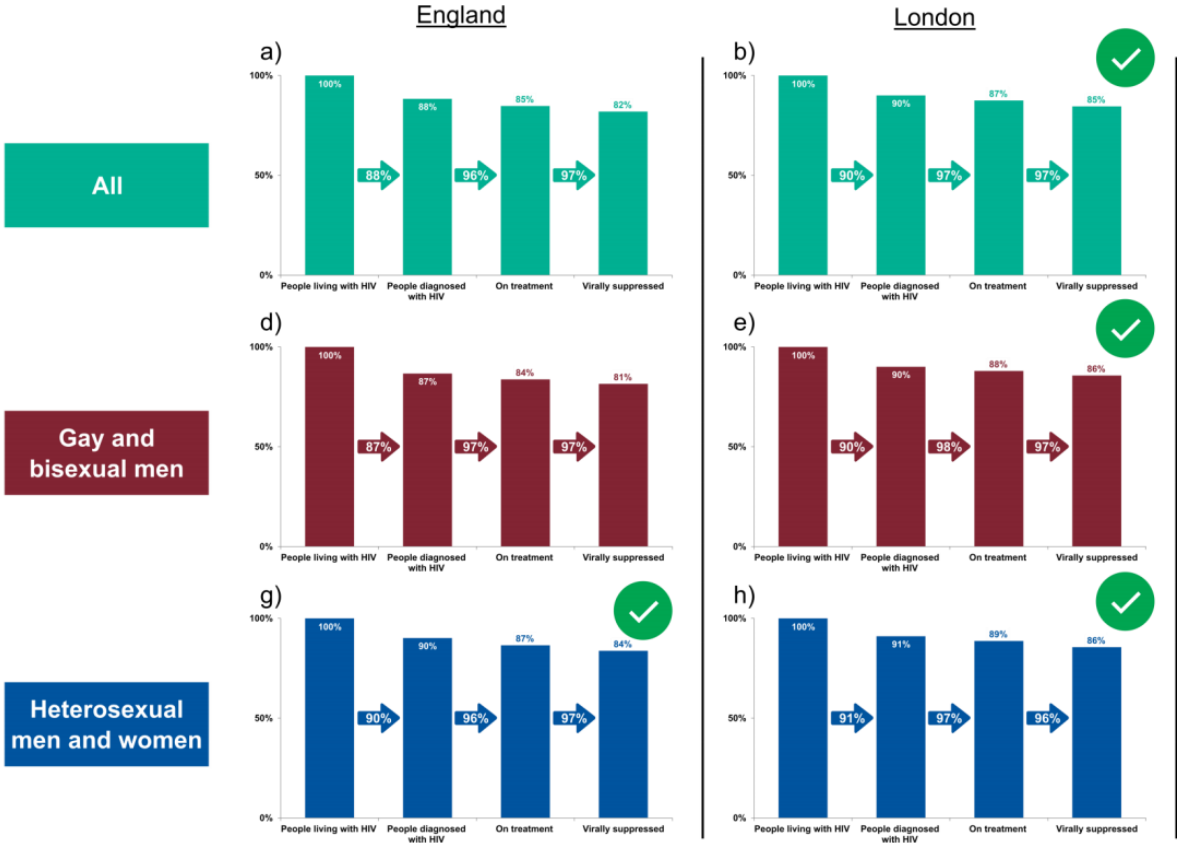
In 2016, London became the third city in the world to achieve the United Nations (UN) 90:90:90 HIV target (90 per cent of people living with HIV diagnosed, 90% of those diagnosed are on treatment and 90% of those on treatment have an undetectable viral load) attaining 90:97:97 (88:96:97 for England as a whole)(1). New HIV diagnosis among gay, bisexual and other men who have sex with men (MSM) have also fallen for the first time since the epidemic began 30 years ago(1).

Figure 18: The continuum of HIV care by region of residence and risk group, England: 2016



This remarkable progress is a result of a combination of interventions. We briefly outline two of these which utilise anti-retrovirals for the prevention of transmission and acquisition of HIV.

Preventing transmission: Treatment as Prevention and "U=U".

Following the introduction of anti-retroviral therapy (ART) in the 1990s, it was observed that a reduction in the HIV viral load (VL) among people living with HIV was associated with a reduction in the risk of HIV seroconversion among their HIV negative partners (2, 3). In 2008, driven by a need to protect people living with HIV from criminalisation for consensual sex, Swiss experts released the following (initially) controversial statement: "*HIV-positive individuals not suffering from any other sexually transmitted disease and adhering to an effective antiretroviral treatment (a blood viral load that has been consistently undetectable for more than six months) do not transmit HIV sexually*"(4). This paved the way for discussion around Treatment as Prevention (TaSP) and several trials to provide evidence to support this statement.

The largest of these, HPTN 052,(5) recruited 1763 serodifferent (homosexual and heterosexual) couples and randomised the HIV positive partner to receive early or delayed ART(5). An interim analysis showed a 96% reduction of HIV transmission within couples in the early ART group and no transmissions when the VL was undetectable. In the observational PARTNER study(6) more than 58,000 episodes of sex without condoms were reported by the 485 heterosexual and 282 MSM serodifferent couples recruited. There were no HIV transmissions observed when the HIV positive partner had an undetectable VL(6). A third study among 358 serodifferent homosexual men also found no transmissions during 17,000 sex acts when the partner with HIV had an undetectable VL(7).

As a result of these studies, the Undetectable = Untransmittable (U=U) message, endorsed by more than 400 organisations from 60 different countries, was launched. The message is simple: a person living with HIV, on treatment who has had an undetectable viral load for over six months cannot transmit HIV to their sexual partners. The effect of the campaign on the mental health of those living with HIV cannot be underestimated- both by assuring their partners that they do not need to fear infection and to help reduce stigma(8).

Preventing acquisition: Pre-Exposure Prophylaxis (PrEP)

The U=U message helps those living with HIV have greater control over their sexual health and risk of transmission, however, there is a need for those who are HIV negative but at risk of acquiring HIV to have control too. Pre-exposure prophylaxis (PrEP) is the use of antiretrovirals by someone without HIV in order to reduce their risk of acquiring the infection if exposed. Currently, oral PrEP using Emtricitabine and Tenofovir is the most commonly used PrEP.

PrEP can be highly effective when taken correctly, with an 86% reduction in HIV acquisition seen in the PROUD(9) and IPERGAY(10) studies. Oral PrEP has been shown to be effective among a range of key populations including MSM and transgender women(9-11), people who inject drugs (PWID)(12) and heterosexual men and women(13, 14). Efficacy varies depending on adherence(15, 16) but may also be influenced by other factors such as the presence of bacterial vaginosis in the case of vaginal preparations of tenofovir(17).
Oral PrEP is generally well tolerated. Approximately 10% of people have described a "start up syndrome" consisting of gastrointestinal symptoms (nausea, abdominal pain, flatulence and vomiting) and non-gastrointestinal symptoms (dizziness and fatigue) which tend to occur within the first month and resolve by three months(18) without the need to stop PrEP. Longer term concerns include a mild, non-progressive and reversible reduction in creatinine clearance, (which is more pronounced in those aged over 40 years and those with predisposing renal dysfunction), and a reversal reduction in bone density by 1-2% (with no long term data on bone health or evidence of increased fracture risk). Thus, draft UK PrEP guidelines recommend an annual estimated glomerular filtration rate (eGFR) in those under

40 years with an eGFR greater than 90mL/min at baseline, biannually if eGFR is 60-90mL/min, aged >40 years or concomitant risk factors for renal function and specialist input should be sought on a case by case basis for those with an eGFR<60mL/min. Patients should be informed of the risk of reduced bone mineral density following 48 weeks of treatment but no routine monitoring is required in those with no additional risk factors.(BHIVA PrEP consultation guidelines)

Currently, access to PrEP in Scotland is free via the NHS. In Wales it is accessed via the PrEPared project. In England, PrEP access is via the PrEP Impact trial or self-sourcing (and self-funding) the drug (it is legal to buy generic PrEP online, sourced from outside the EU, so long as this is for personal use). PrEP is not currently available in Northern Ireland. With an unknown number of individuals self-sourcing PrEP it is important that all physicians remain vigilant, particularly with regards to monitoring renal function and to the possibility of any drug-drug interactions, which can be checked at www.hiv-druginteractions.org.

In England, we are at a turning point in the HIV epidemic and the combination of frequent testing, PrEP and treatment as prevention are undoubtedly instrumental in this. However, key inequalities exist with regards to HIV outcomes, awareness and knowledge of HIV and prevention, and access to services and further work will need to be done to strengthen prevention efforts. Clinicians working across hospital specialties are crucial to this in identifying those who may benefit from PrEP and the U=U message, especially in an era of reduced access to sexual health clinics.

KEY LEARNING POINTS

1. Undetectable = Untransmittable: a person living with HIV, on treatment, who has had an undetectable viral load for over six months cannot transmit HIV to their sexual partners.
2. Pre-exposure prophylaxis (PrEP) can be highly effective when taken correctly, with an 86% reduction in HIV acquisition and is effective among a range of key populations including MSM and transgender women, people who inject drugs (PWID) and heterosexual men and women.
3. Access to PrEP varies throughout the UK; in Scotland it is freely available on the NHS, in Wales via the PrEPared project and in England via the Impact trial. It is not available in Northern Ireland. For those who are unable to access PrEP through these means, PrEP is often self-sourced via www.iwantprepnow.co.uk.
4. PrEP is well tolerated with the majority of mild symptoms resolving by 3 months. Renal monitoring in some patients may be necessary.

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