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POSTNOTE

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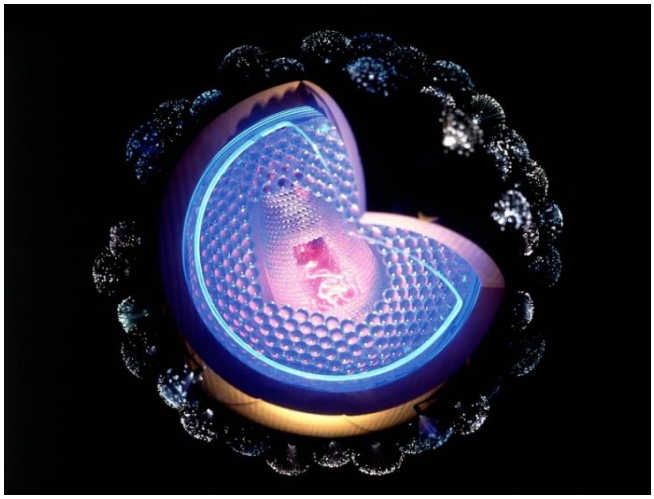
HIV Prevention in the UK



Preventing HIV is a priority for research and public health. Research developments and the trends in the nature of the epidemic mean that policy is continually revised in order to educate the public, reduce transmission of the virus and treat those affected. This note describes patterns of infection and policies to increase HIV testing. It also summarises evidence for using antiretrovirals as a preventive measure.

Overview

- People with HIV who receive appropriate treatment have a near-normal life expectancy and are very unlikely to transmit the virus to others.
- The proportion of people receiving a late diagnosis was 47% in 2012. An estimated 22% of people with HIV in the UK are unaware of their infection. Increasing HIV testing is important so that treatment is given and onward transmission prevented.
- Successful prevention depends on a combination of testing, treating and behaviour change (safer sex practices).
- Giving antiretroviral drugs to those at risk of catching HIV (pre-exposure prophylaxis) could reduce infections. This is being implemented in the US, and research is underway to collect UK-specific data.
- There are concerns that the separation of commissioning HIV treatment and prevention has negatively impacted patients.

Background

The Human Immunodeficiency Virus (HIV) damages specialised cells of the immune system. If HIV is untreated the immune system becomes unable to function. People with HIV are thus more susceptible to other secondary conditions, notably tuberculosis, pneumocystis and some cancers. The presence of these conditions meets the definition of acquired immune deficiency syndrome (AIDS).

There is no cure or vaccine for HIV. Research is underway to achieve a 'functional cure' - no evidence of viral replication when treatment has ceased – but this may not be possible. Daily oral anti-retroviral drugs are very effective for the long-term management of HIV and early treatment results in a near normal life-expectancy. The stage of infection is assessed by measuring the number of immune cells in the blood that HIV targets (called a CD4 count). Research is underway to define the threshold for starting treatment but it usually begins when the count is lower than 350 cells/mm^3. However, almost half of HIV cases are diagnosed late or remain undiagnosed, particularly among black Africans and men who have sex with men (MSM). Box 1 details patterns of HIV infection.

Overall prevalence in the population in 2012 was 1.5 per 1,000, but much higher in MSM (47 per 1,000 [80 per 1,000 in London]) and heterosexual black Africans (men: 26 per 1,000, women: 51 per 1,000). In 2012, 47% of those receiving a new HIV diagnosis had passed the point at which treatment should begin. People diagnosed late have a tenfold risk of dying within a year of diagnosis, with the risk particularly marked for those aged over 50.[1] Public Health England (PHE) estimates the annual cost of HIV treatment and care at £858m. It calculates that each infection prevented saves £320,000 in lifetime care costs.[1] HIV surveillance informs the targeting of prevention measures, testing and treatment.

Approaches to preventing HIV

There are two approaches to preventing transmission:

- **Changing behaviours** to encourage safer sex practices (promoting condom use, reducing the number of sexual partners) and by encouraging people at increased risk (particularly after unprotected sex with a new partner) to test regularly. One modelling study showed that condoms strongly limit HIV transmission in MSM.[2] However, there

Box 1. The UK HIV epidemic – latest trends[1]

In 2012, an estimated 98,400 people were living with HIV, 22% of whom were unaware of their infection.[3] There were 6,360 new diagnoses, 490 deaths among those with HIV and 390 cases of AIDS. The number of new diagnoses has continued to decline overall since 2005, but has been rising among MSM since 2007.

- **Men who have sex with men:** over half of the new diagnoses made in 2011 were in MSM, the highest number ever reported and 70% higher than in 2001. An estimated 41,000 MSM had the virus, of whom 7,300 were unaware of their infection. Most infections were acquired in the UK (84%).
- **Heterosexuals:** of the 2,580 new diagnoses in 2012 (1,530 women and 1,050 men), 52% were acquired in the UK, up from 27% in 2002. Notably, 57% of heterosexuals infected were black Africans.
- **Other transmission routes:** cases from other routes (mother-to-child and injecting drug users) form a small proportion, because of successful initiatives on prevention, testing and treatment.

have not been any systematic evaluations of the direct effectiveness of national behavioural interventions.

- **Medical treatments** using antiretroviral drugs. As discussed later these can be used: to reduce transmission of the virus; to prevent the infection taking hold after exposure; prophylactically to prevent infection.

Increasing access and take up of testing

In the UK, HIV tests (Box 2) are recommended and routinely offered as part of ante-natal screening (take up 96%) and in sexual health clinics (take up 69% overall, 84% in MSM). They are also widely offered in community settings and increasingly by post. Although 900,000 tests were carried out in sexual health clinics in England in 2012, 29% of attendees did not have a test. Reducing late diagnosed and undiagnosed HIV requires increasing testing coverage in a wider variety of settings, in areas of high prevalence. The main reason cited for not testing is a person's perception that they are not at risk. Others include privacy concerns, stigma, transport costs to attend clinics, restricted clinic opening hours and long waiting times.

Policies to increase HIV testing

Testing in high prevalence areas

Routine HIV testing is cost effective in high prevalence areas, where HIV affects at least 2 in 1,000 people. Sixty-four local health authorities, thirty-two of which are in London, have high HIV prevalence. Public Health England state that in these areas, testing should be offered routinely to adults (aged 15-59) registering in general practice and for all general medical admissions to hospital.[1] HIV testing is also recommended for any adult presenting with a glandular fever-like illness since this might indicate an HIV infection.

Reaching high risk groups

Guidance from the National Institute for Health and Care Excellence (NICE) specifies how take up of testing in black African and MSM groups can be increased, by offering wide-scale testing in primary, secondary and emergency care settings and addressing common misconceptions about HIV treatment and care. The Terrence Higgins Trust is running a three-year Department of Health-funded programme (HIV Prevention England) targeting gay men and black African communities. It includes campaigns to encourage regular testing and to promote National HIV Testing Week (every November). It will also collect data on which prevention approaches are most effective.

Box 2. HIV testing

A person infected with HIV produces antibodies against the virus. Most tests determine whether these are present in blood or saliva. They are cheap and are highly sensitive, giving results within 20 minutes. Other tests check for the presence of HIV's genetic material. These are expensive and complex, so their use is confined to screening blood donations and babies born to HIV-positive mothers. New fourth generation tests use antigen and antibody detecting technology and are better at detecting recent infections.

Home testing

The 1992 ban on selling home testing kits for personal use will be abolished in April 2014. A Terrence Higgins Trust survey found that some people at risk of HIV would be more likely to test, or to test more regularly, if they could do so at home. Perceived benefits are choice, convenience and anonymity. Legal home tests are already available in the US, New Zealand, Hong Kong and the Netherlands. The test approved in the US gives a result from a saliva sample within 20 minutes. If a home test is positive a confirmatory test is needed. HIV testing kits in the UK must meet quality and safety standards set out in European and national legislation and will be available for purchase in pharmacies. Home sampling, by sending a saliva or blood sample to a laboratory, is already legal in the UK and is also advocated by charities as a way of encouraging increased testing. Results are available by telephone and positive outcomes confirmed with a blood test in a clinical setting.

Treating HIV

Early diagnosis is key to reducing the risk of HIV transmission to sexual partners and from pregnant women to their babies. Late diagnoses were lowest in men who have sex with men (34%), but more common for heterosexual men (65%) and women (57%).[1]

Vaccines

There is no vaccine for HIV, despite testing of over 30 candidates. Research continues but experts think that it is very unlikely that one will be available within the next decade. Designing a vaccine is difficult because there are several HIV subtypes, and frequent mutations, and unlike other viruses for which vaccines have been developed (such as hepatitis B), there is no natural response to copy.

Anti-retroviral drugs

There are several types of antiretroviral drug. Some prevent the virus entering a host cell while others interfere with the viral life cycle. To minimise resistance, at least three different drugs are combined into one or more pills taken orally every day. Side-effects are common and many resolve within weeks, but more serious effects can be

improved by changing drug combinations. Antiretrovirals are also formulated as gels or creams.

Drug resistance

HIV, like most viruses, changes or mutates. Some mutations change the virus so that it no longer responds to antiretrovirals and continues to reproduce in their presence. This is termed ***acquired resistance***. Newly-diagnosed people may have drug-resistant forms of HIV, passed from the person that infected them, called ***transmitted resistance***. The consequence of either is that resistance may result in treatment failure and limit treatment options.

Resistance is tracked by the UK HIV Drug Resistance Database. The prevalence of resistance in those already treated with antiretroviral drugs is falling, down from a peak of 78.5% in 1999 to 37.1% in 2010, as surveillance data informs clinical care. However, the proportion of people not yet treated with antiretrovirals, but infected with a transmitted drug-resistant form of HIV, is increasing by a small but significant margin. In 2006, transmitted resistance in this group was at its lowest level, at 7%, but increased to 8.2% by 2010. A recent study showed that HIV-positive patients who had not yet received anti-retroviral drugs may increasingly be the source of transmitted resistance.[4] As a consequence, guidelines recommend that newly diagnosed people and those for whom treatment is failing are tested for the presence of resistant strains, so that suitable drugs can be selected. Continued monitoring of resistance is needed to track HIV-resistant strains and to assess the need for new classes of antiretrovirals.

Treatment costs

As the cohort of HIV-positive people in the UK ages, the spend on HIV drugs and other costs of providing specialist care and treatment is increasing. This will change over the next five years as patents on branded drugs expire.

Preventing HIV with antiretrovirals

There is increasing focus on strategies that employ antiretrovirals to prevent HIV, targeted at both HIV-positive and HIV-negative individuals (to reduce transmission either before or directly after exposure to the virus). This section focuses on the use of anti-retroviral drugs to:

- suppress transmission of HIV by those already infected
- minimise the risk of infection in those who may be, or who have been exposed to HIV.

Post-exposure prophylaxis

A four-week course of antiretrovirals which can be obtained only from sexual health or A&E units under certain circumstances, can minimise the chance of an HIV infection becoming established after an exposure (such as a broken condom or needlestick incident). The sooner treatment is started the more likely it is to work. Ideally it should begin within 24 hours; after 72 hours is too late. They have serious side effects and the course must be completed to be effective. For these reasons, post-exposure prophylaxis is considered a last resort treatment in an emergency rather than a substitute for safer sex practices and other preventive approaches. There is conflicting evidence as to whether post-exposure prophylaxis increases risky behaviour.

Pre-exposure prophylaxis

This prevention approach (known as PrEP) involves HIV-negative people at risk of becoming infected taking a regular course of antiretroviral drugs prior to possible exposure. Antiretroviral drugs have been (and are still being) assessed against a placebo control in several clinical trials administered either:

- locally, formulated as vaginal gels (termed microbicides, see Box 3) or released from intravaginal rings
- systemically, using tablets taken orally.

PrEP has a preventive effect by reducing viral replication and minimising the chance of a permanent infection developing. A daily oral dose of the antiretroviral drug Truvada is licensed as PrEP in the US, but not in Europe. It is not yet available on the NHS, but is being assessed in a pilot study funded by the Medical Research Council and Public Health England. This will determine whether PrEP is cost-effective as part of a comprehensive prevention strategy.

Clinical trials of pre-exposure prophylaxis

Trials so far show that PrEP is biologically effective, but unlike condoms, does not protect against other sexually transmitted infections. A robust analysis calculated that condoms offer at least a 94% reduction in the risk of catching HIV for heterosexuals and MSM.[5] The estimates from the PrEP trials range from 0 to 73%, the reasons for this range are discussed below. All the trials included a placebo and participants were counselled that they could be on placebo, advised on preventing HIV and given condoms. Evidence from randomised placebo-controlled trials showed that the following groups benefitted from oral antiretroviral:

- **MSM:** the level of protection correlated with adherence to taking daily Truvada. The risk of contracting HIV was reduced on average by 44%. This increased to 73% when taking pills on at least 90% of days in the trial.
- **heterosexual couples:** where one partner is HIV-negative and the other is HIV-positive (serodiscordant). The PARTNERS PrEP trial found that daily oral tenofovir or Truvada given to the HIV-negative partner reduced infections by 67% and 75%.[6] Serodiscordant couples in this trial showed good adherence to the drug regimen.
- **young heterosexual adults:** daily oral Truvada reduced the risk of men and women contracting HIV by 63%.[7]
- **intravenous drug users:** daily oral tenofovir reduced the risk of contracting HIV (men and women) by 67%.

Two other trials of daily oral Truvada or tenofovir failed to show benefit. Both were conducted in women at risk in sub-Saharan Africa. One trial showed that an antiretroviral gel containing 1% tenofovir used by heterosexual women before and after sex reduced the risk of HIV by 39%.[8],[9] Women who used the gel as directed were much better

Box 3. Antiretroviral microbicides
Microbicides are drugs used locally, applied to the vagina or rectum to protect against sexually transmitted infections, including HIV. Their mode of action is analogous to oral antiretrovirals, but some formulations provide a physical barrier so that the virus cannot access target cells. They are under development and being tested in trials (see below), but the ideal microbicide would offer long-lasting protection (several days or weeks per application), be inexpensive, easy to apply and have no adverse impacts on a woman's reproductive health. A benefit of microbicides is that they offer women the choice to protect themselves without their sexual partner's knowledge or consent. This is especially relevant to societies where women are disempowered, where condoms are not likely to be used for cultural or other reasons or where having multiple sexual partners is a social norm.

protected, with the risk reduced by 54%. A second trial assessing the use of daily tenofovir vaginal gel failed to show any benefit, but only a third of women had any detectable drug in their system.[10] A third trial is underway to assess use of gels before and after sex, results are due in 2015. Two other trials are assessing continuous release of dapivirine from an intravaginal ring, also reporting in 2015. Other trials of male-to female-transmission using oral antiretrovirals showed no protective effect and side-effects were reported. One trial ended early as there were as many HIV infections in the treatment as the placebo group. The varied levels of adherence to the drug regimen in different populations and social groups emphasises the importance of collecting evidence in specific groups of people.

PrEP: Possible Impacts and Challenges
There is only one drug available as PrEP which must be taken daily. It does not provide full protection, and does not protect at all against other sexually transmitted infections. There are concerns about the cost of the drugs and the cost of delivering them, at a time when funding to implement existing prevention policies is limited. There is scientific uncertainty whether the availability of PrEP would affect other behaviours. One concern is that if people know they are taking PrEP they may be more likely to engage in risky behaviours (more partners, decreased condom use), less likely to take the drug as prescribed and thus be more likely to contract HIV and other sexually transmitted infections such as hepatitis. Finally, there are concerns that poor adherence to PrEP could facilitate resistance, limiting the drugs that could be used to treat an individual. Furthermore, existing drug resistance might make PrEP less effective. This is because resistance in HIV-positive people could lead to the transmission of virus which PrEP cannot protect against. Recent research does not support this, but monitoring is needed to track resistance in PrEP studies.

The number of new HIV diagnoses is relatively stable overall but reported infections are rising in some populations due to increased testing. No single prevention method (such as condoms) can control the epidemic. PrEP is biologically effective, and could enable providers to offer comprehensive risk reduction to those not using condoms all the time. Public Health England considers that PrEP is unlikely to reduce HIV transmission in the UK.[1]The Medical Research Council's Clinical Trials Unit is running a trial to assess the effect of PrEP in MSM in the UK, in collaboration with Public Health England.[11] Trial participants are randomly split into two groups, one of which receives Truvada straightaway and the other after 12 months. This allows researchers to compare any differences that PrEP might make to sexual activity. The trial will conclude in 2016.

The Expert Advisory Group on AIDS (which advises the Chief Medical Officer) and the British HIV Association released a position statement on PrEP in 2013. It recommended that health professionals should discuss with all people living with HIV the impact of antiretrovirals on transmission. It advises that those not taking them but who wish to reduce the risk of transmission should discuss starting therapy for this purpose. The statement specifies clinical guidance (more frequent HIV viral load testing and tests for other sexually transmitted infections) but states that no single method can completely prevent transmission.[12]

HIV policy and impact of NHS reforms

The Department of Health published 'A Framework for Sexual Health Improvement in England', including HIV, in 2013. The 2012 Health and Social Care Act changed the mechanisms for planning, buying and delivering health prevention, clinical and social care in England.

New Arrangements for HIV Services
Since April 2013, most health services are planned and funded ('commissioned') at local level. GP-led groups commission most local hospital care. However, HIV clinical care services are planned by the new body, NHS England and by equivalent bodies in the devolved administrations. HIV social care continues to be commissioned by local authorities, along with HIV prevention and other sexual health services. Many HIV charities and clinician networks are concerned that people with HIV are falling through gaps in the newly established structures and that decisions taken at the national and local levels are not integrated.

Endnotes
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