

Introduction

This briefing paper covers undiagnosed HIV infection and late diagnosis of HIV in the UK. One in five people living with HIV are unaware of their infection, while half of all diagnoses are made 'late'; in other words, when HIV treatment should already have been started (after the CD4 cell count has fallen below 350 cells/mm³).

Undiagnosed HIV infection has two major consequences. Individuals are at greater risk of transmitting HIV to others as they cannot take HIV treatment (which suppresses the virus and greatly reduces the risk of onward transmission) and cannot make informed decisions about their sexual behaviour. Secondly, individuals who are diagnosed late are at risk of serious clinical illness. All people with HIV are undiagnosed for a period of time, while some individuals' infections remain undetected for so long that they are diagnosed late. This briefing begins by addressing the issue in terms of undiagnosed infection, before turning to late diagnosis.

The briefing focuses on the two populations most affected by HIV in England, men who have sex with men (MSM) and black African communities. More research has been done on this issue in relation to MSM. The briefing describes the scale, characteristics and consequences of the problem; it does not address interventions to tackle it.

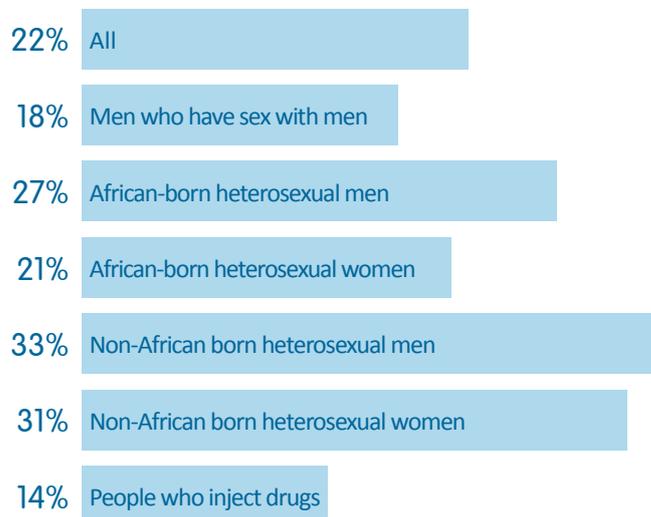
What proportion of infections are undiagnosed?

By its nature, information on undiagnosed infection is challenging to produce accurately. [Public Health England produces estimates](#) based on anonymised blood samples which have been taken for other purposes (e.g. for syphilis testing in GUM clinics; from newborn infants, providing information on pregnant women).

The data are adjusted in the light of other information, such as CD4 cell counts when people are diagnosed and estimates of the size of sub-populations (e.g. the number of African adults living in the country). Known biases are corrected for (e.g. people who attend GUM clinics tend to have higher levels of infection than other people).

For 2012, it was estimated that 22% of people living with HIV were unaware of their infection. There are inequalities between different demographic groups – heterosexual men have the highest rates of undiagnosed infection. The routine offer of HIV testing in antenatal settings probably

Proportion of people living with HIV who are undiagnosed: United Kingdom, 2012



Source: Public Health England

contributes to a smaller proportion of heterosexual women having undiagnosed infection, in comparison with heterosexual men.

Around 4,300 African women and 3,000 African men are living with undiagnosed HIV. [An African community study](#), conducted a decade ago, found that of those individuals with undiagnosed HIV, just over half had never tested and a third said their last HIV test result was negative.

Around 7,300 gay and other men who have sex with men have undiagnosed HIV. Although the *proportion* of infections that are undiagnosed is relatively low in this group, the *number* of individuals concerned is large. [Research conducted a decade ago](#) in gay commercial venues found that 62% of the men with undiagnosed infection believed themselves to be HIV negative.

The impact of undiagnosed infection on HIV transmission

Reducing undiagnosed infection is vital because an individual can only take HIV treatment if HIV has been diagnosed. Effective HIV treatment reduces HIV viral load, the main biological predictor of the risk of HIV transmission. UK treatment guidelines state that people with CD4 counts above 350 cells/mm³ should be allowed to choose to start treatment in order to reduce their risk of passing on HIV to sexual partners. People who remain undiagnosed – and their partners – are unable to benefit from this recommendation.

UK studies suggest that undiagnosed infection is a major contribution to the spread of HIV in MSM. [A national study](#) found that one third of MSM living with HIV are infectious, with a viral load above 1500 copies/ml. However, the majority (62%) of these men are undiagnosed. [A modelling study estimated](#) that, in 2010, 48% of new infections were acquired from men with undiagnosed primary HIV infection, 34% from men with undiagnosed chronic infection, 10% from men who were diagnosed but not on treatment, and 7% from men on treatment. High rates of partner change are likely to amplify the impact of undiagnosed infection.

Similar estimates are not available for African people in the UK.

How accurate are the figures on undiagnosed infection?

It is possible that the figures for undiagnosed infection are slightly inflated by the phenomenon of people who, having had their HIV infection diagnosed and treated at one clinic, attend a second clinic for sexual health check-ups, without revealing their HIV status. [Individuals may do this](#) to benefit from more convenient services (e.g. opening times) and to avoid disclosing risky sexual behaviour. [Recent research has shown](#) that some GUM attendees with 'undiagnosed HIV' in fact have traces of antiretroviral drugs in their blood and that this occurs in all demographic groups. Public Health England will investigate the scale of the phenomenon and adjust future estimates accordingly.

HIV diagnosis and sexual risk taking

Earlier diagnosis would also give people the opportunity to make informed decisions about their sexual behaviour. Research suggests that most people diagnosed with HIV reduce their risk behaviour, in the short term at least. [A meta-analysis of American studies](#), conducted with both heterosexuals and men who have sex with men, found that high-risk sexual behaviour was 53 to 68% less frequently reported in the months following diagnosis.

However, it is unclear whether this kind of behaviour change is sustained. Only a few studies have followed the same individuals for more than a year after being diagnosed and the results are contradictory. [A study of Kenyan sex workers](#) found that reductions in risky behaviour were maintained for several years after diagnosis. [A study with Dutch gay men](#) observed a fall in unprotected sex immediately after

diagnosis, but four years later risk behaviour had returned to pre-diagnosis levels.

Of note, these kind of studies only rarely collect enough information to tell us about risk-reduction strategies which rely on knowledge of HIV status – for example, only having unprotected sex with partners who also have HIV ('seroadaptation' or 'serosorting') or, in the case of MSM, choosing sexual position according to each partner's HIV status ('strategic positioning').

Undiagnosed primary infection

It is useful to consider specifically the impact of undiagnosed primary infection. Primary infection refers to the first few months of infection, when individuals have exceptionally high viral loads in blood and in genital fluids. [It is estimated](#) that the per-act risk of HIV transmission is 26 times greater during the first three months of infection than during chronic infection.

By definition, a person with primary HIV infection has recently engaged in a behaviour that led him or her to acquire HIV, and that behaviour may be continuing. However, because primary infection only lasts a few months, there may be fewer opportunities for transmission than during several years of chronic infection.

It is difficult to diagnose individuals during primary infection. [All HIV diagnostic tests](#) have a 'window period' during which they cannot detect a recently acquired infection. While most individuals have symptoms of HIV seroconversion, these may be mistaken for the 'flu or glandular fever' by doctors. People at risk of HIV infection are often unaware that a sore throat, rash and fever can be symptoms of HIV seroconversion (especially if the symptoms occur together) and may not seek health care.

Increasing the frequency of HIV testing is likely to increase the number of infections diagnosed early ([see *How often should people test?*](#) below).

[A study of London gay men](#) diagnosed during primary infection found considerable behaviour change in the three months following diagnosis. The number always using condoms during insertive anal intercourse increased from 31 to 61%; two-thirds reduced partner numbers; and there were far fewer diagnoses of sexually transmitted infections. The researchers argue that even short-term behaviour change at this time of increased infectivity is likely to prevent new HIV infections.

Undiagnosed HIV infection

Late diagnosis of infection

A 'late' diagnosis is one which is made at a point in time after which HIV treatment should have been started. In 2012, among those newly diagnosed, 47% were diagnosed late (with a CD4 cell count below 350 cells/mm³), including 28% who were diagnosed very late (with a CD4 cell count below 200 cells/mm³).

Inequalities are apparent – while 34% of gay and other men who have sex with men were diagnosed late, rates are much higher in heterosexual men and women. They are particularly high amongst black African heterosexuals, many of whom are likely to have acquired HIV before their arrival in the UK. In 2012, 66% of black African men and 61% of black African women were diagnosed late.

Older adults are over-represented amongst those diagnosed late – 63% of people who are diagnosed over the age of 50 have CD4 cell counts lower than 350 cells/mm³.

Over the past decade, the proportion of individuals diagnosed late has declined significantly, from 58% in 2003 to 47% in 2012. The decline has been seen in all exposure groups, but especially in MSM.

The public health performance of local authorities will be judged, in part, on actions to reduce late diagnosis of

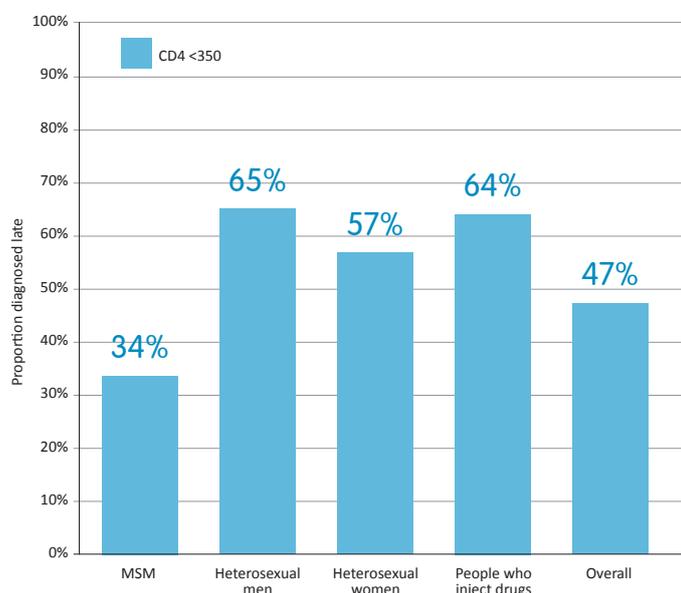
HIV. The Public Health Outcomes Framework includes the proportion of people newly diagnosed with HIV who have a CD4 count below 350 or who develop AIDS within three months of diagnosis as an outcome 'indicator'. This is intended to focus decision makers' attention on the issue of HIV testing.

Because of this, Public Health England publishes data for each local authority on late diagnosis, highlighting disparities between different areas. For example, the neighbouring London boroughs of Tower Hamlets, Hackney and Newham have late diagnosis rates of 33, 45 and 60% respectively. Whereas Blackpool has a late diagnosis rate of 29%, in Salford, 51% of diagnoses are late.

Reducing late diagnosis is important because not taking treatment until the immune system is severely weakened increases the chances of developing serious, life-threatening illnesses.

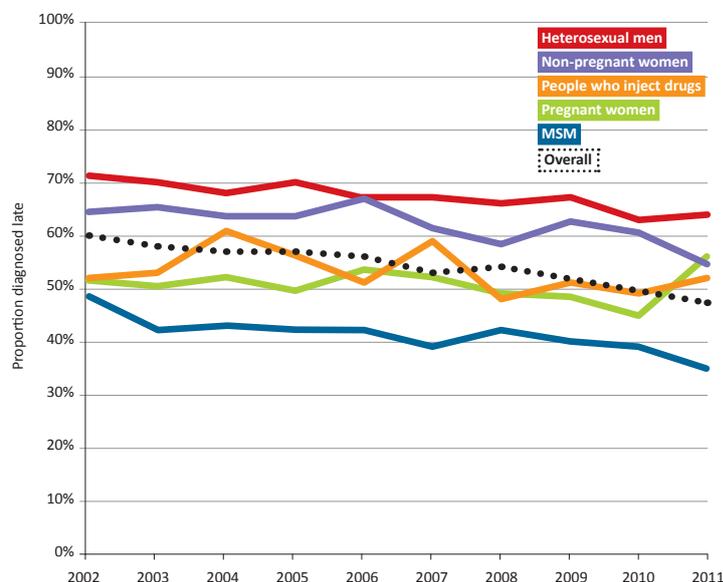
Analysis of the SMART study showed that people who delayed treatment until their CD4 cell count was below 250 cells/mm³ had a four-fold greater risk of opportunistic infections and serious non-AIDS clinical events, compared to people who started treatment with a CD4 cell count above 350 cells/mm³. A ten-year analysis of deaths in people with HIV in the United Kingdom found that individuals diagnosed with a CD4 cell count below 350

Late diagnosis of HIV infection by exposure group: United Kingdom, 2012



Source: Public Health England

Trends in late diagnosis by exposure group: United Kingdom, 2002-2011



Source: Public Health England

cells/mm³ were ten times more likely to die of AIDS. The researchers estimate that 81% of all AIDS-related deaths and 61% of all non-AIDS-related deaths were caused by late HIV diagnosis. [Moreover, there is a particular risk of mortality](#) for older adults who are diagnosed late.

However, the risk of illness and death is concentrated in the first year after being diagnosed – if people start treatment and get through the first year, longer-term outcomes are good.

[In terms of life expectancy](#), people starting HIV treatment with a CD4 cell count below 100 cells/mm³ live 15 fewer years than people starting treatment at a CD4 cell count between 200 and 350. People starting treatment with between 100 and 200 cells/mm³ live for 12 fewer years.

Each new case of HIV infection costs the NHS between £280,000 and £360,000 over a lifetime. But [costs are greatest for individuals diagnosed late](#) – in the first year after diagnosis, spending is doubled for those diagnosed with a CD4 count lower than 200 cells/mm³. This is largely due to increased inpatient hospital care costs, as well as the cost of extra investigations, immediate antiretroviral therapy and drugs for medical conditions caused by immunosuppression.

Late diagnosis is also a problem for onward transmission. As an individual becomes increasingly immunocompromised, viral load rises, so [he or she is more infectious](#) until effective treatment is taken.

How often should people test?

Regular and frequent testing is a good way for HIV infection to be identified before a substantial decline in CD4 count. While there has been a significant rise in the uptake of HIV testing in recent years, the [2010-12 National Survey of Sexual Attitudes and Lifestyles](#) found that among men who have sex with men, only 27% had tested in the previous year and 52% had done so in the past five years. Less than half the black African men (44%) and black African women (46%) had tested in the previous five years. Across all demographic groups, people with more sexual partners were more likely to have tested.

Public Health England recommends that MSM should have an HIV test at least once a year, and every three months if having unprotected sex with new or casual partners. The National Institute for Health and Care Excellence (NICE) has a similar recommendation.

Facilitators and barriers to testing

Research has identified a range of factors that affect people's motivation to take an HIV test. [Studies conducted with men who have sex with men](#) have found that new circumstances, such as a new relationship or unexplained health problems, can prompt some people to test. However, individuals who test regularly tend to see it as the 'responsible' thing to do and are not necessarily motivated by specific risky incidents. While many people test in order to eliminate the uncertainty of not knowing their HIV status, others may respond to uncertainty with denial – for example, through assessing their own behaviours in a way that minimises the possibility of an HIV-positive status. Individuals may fear that discovery of an HIV-positive status would mean facing difficult decisions and responsibilities, especially in relation to sexual partners.

The stigma associated with HIV infection is identified as a barrier to testing in all populations, but [especially so in black African communities](#). People fear exclusion and social isolation as consequences of being diagnosed with HIV. Many people associate HIV with promiscuity or unfaithfulness, and see themselves as being at very low risk of infection – [many are unaware of the high rates of HIV infection](#) in UK African communities. Other urgent priorities (economic survival, immigration problems, childcare responsibilities etc.) may take precedence over health-seeking behaviour, especially as not everybody is aware of the value of a test in the absence of symptoms or knows where to get tested.

Many people with undiagnosed HIV who have symptoms go to GPs and other health services, but may be treated by clinicians who are reluctant to recommend an HIV test, or who do not consider the possibility of HIV infection (although [guidelines recommend HIV testing if a patient has an 'indicator condition'](#)). Research suggests that more routine or 'opportunistic' offers of HIV tests by healthcare professionals (outside of sexual health services) are acceptable and would facilitate greater uptake of testing, especially in African communities.

In relation to black African and Caribbean people, PHE recommends that individuals who have unprotected sex with new or casual partners should test regularly, but the frequency is not defined. [The National AIDS Trust has argued](#) for a recommendation of an annual test for all sexually active African people in the UK.

But some researchers suggest that these recommendations are too conservative and that frequency of testing needs to be based more precisely on the incidence of new infections in a community. [A mathematical model based on the American health system found that](#), in a community with an incidence of 0.01%, the most cost-effective testing frequency is once every 2.4 years. If the incidence is 0.1%, testing should occur every nine months. In a community with an incidence of 1%, the optimal testing frequency is every three months. Reliable estimates of incidence among African people in the UK are currently lacking, but [may be around 0.5% in MSM](#).

Key points

- One in five people living with HIV are unaware of their infection.
- Half of all diagnoses are made 'late'; in other words, when HIV treatment should already have been started. Rates of late diagnosis are especially high in black African men.
- Undiagnosed infection has significant implications for public health, as individuals may have very high HIV viral load, increasing the risk of onward HIV transmission.
- Individuals with undiagnosed HIV also risk severe immunosuppression, serious illness and reduced life expectancy, as well as greater costs to health services.
- Improvements in HIV testing practices are required in order to reduce undiagnosed infection and late diagnosis.

Further reading

Public Health England. *HIV in the United Kingdom: 2013 Report*.

Cairns G. *Tales of the Late Diagnosed*. HIV Treatment Update, winter 2013.

Phillips AN et al. *Increased HIV Incidence in Men Who Have Sex with Men Despite High Levels of ART-Induced Viral Suppression: Analysis of an Extensively Documented Epidemic*. PLoS One 8(2), 2013.

Fakoya I et al. *Increasing the uptake of HIV testing to reduce undiagnosed infection and prevent transmission among black African communities living in England: Barriers to HIV testing (Final Full report)*. National Institute for Health and Care Excellence 2011.

Lorenc T et al. *HIV testing among men who have sex with men (MSM): systematic review of qualitative evidence*. Health Education Research 26 (5), 2011.

Written by Roger Pebody, November 2013.

Thanks to Valerie Delpech (Public Health England), Fiona Burns (University College London), Joanna Moss (MBCARC), Jabulani Chwaula (BHA) and Cary James (Terrence Higgins Trust) for their comments and feedback.