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CLINICAL REVIEW

HIV testing and management of newly diagnosed HIV

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HIV infection in the United Kingdom remains a public health challenge; in 2012 an estimated 98 400 people were living with HIV infection, with 1 in 5 cases undiagnosed. The prognosis for those with a diagnosis of HIV is broadly excellent. Most patients with newly diagnosed HIV infection should prepare for a normal, healthy, and productive lifespan.

UK guidance on HIV testing,[1] published in 2008, encouraged the normalisation and expansion of HIV testing. As a result more testing is now being undertaken in non-specialist settings, with an increase now being seen in the number of cases being diagnosed outside specialist services.

The purpose of this review is to provide an evidence based summary to support primary and secondary care clinicians in delivering HIV testing and to guide them in the initial management of patients with newly diagnosed HIV infection. Although we focus on the situation in the UK, many of the principles apply to populations worldwide. Globally, undiagnosed and late stage diagnosed HIV infection is a feature of many epidemics in the developed world. Some countries face different problems. In the United States, for example, poor linkage to (and retention in) specialist care of patients with known HIV infection is a greater problem than in western Europe. Guidance for a specific country must be responsive to the specifics of the epidemiology of HIV infection and clinical outcomes within the local health system.

What is the current epidemiology of HIV infection in the UK?

The advent of combination antiretroviral therapy has transformed the prognosis of patients with HIV infection. People with a diagnosis of HIV infection before moderate to severe immunosuppression occurs should now anticipate a normal life expectancy.[2]

The prevalence of HIV infection in the UK has risen steadily and, in 2012, stood at an estimated 98 400 people (1.5/1000 population). The epidemic remains concentrated in, but is not restricted to, higher risk groups—men who have sex with men, and heterosexuals from areas of high endemicity, notably sub-Saharan Africa. There is also notable variation in prevalence geographically, with most people living with HIV residing in large urban centres.[3] In 2012, more than 6000 people were newly diagnosed as having HIV infection, an increase on 2011. The highest number of annual diagnoses ever was recorded in men who have sex with men (MSM), at 3250 (51% of total). Heterosexuals comprised 45% of all new diagnoses in 2012.[3] Of these, 52% were believed to have acquired their infection in the UK (including 48% of heterosexuals born abroad)—a figure that has risen from 27% in 2002.[4]

Timely linkage to care and excellent clinical outcomes are consistently shown in the UK, with 95% of people with a diagnosis currently accessing specialist care, of whom 88% are receiving antiretroviral therapy. Eighty six per cent of this group has an undetectable viral load—a surrogate marker of treatment success.[3]

Why diagnose the undiagnosed, and why the hurry?

The epidemiology of HIV in the UK remains marred by a stubborn undiagnosed fraction, and by a high proportion of late diagnoses.

Undiagnosed HIV infection

An estimated 22% of people living with HIV infection do not know their status (ranging from 18% in men who have sex with men to 30% in male heterosexuals).[3] Undiagnosed HIV infection contributes disproportionately to ongoing transmission, with onward infection up to 3.5 times greater in this group based on mathematical modelling and behavioural and surveillance data.[5] Knowledge of status reduces risk behaviours and allows partners to access testing.[6] Importantly, in several observational studies antiretroviral therapy has been shown to reduce transmission[7 8] and in one randomised controlled trial was definitively shown to reduce transmission from index case to partner by up to 96%.[9] Access to antiretroviral therapy is contingent on knowledge of status.

Late diagnosis of HIV infection

European consensus of late HIV diagnosis was arrived at in 2009 and defined as a CD4 count at diagnosis of <350 cells/μL.[10] It is generally agreed across international guidelines that all patients ought to have started antiretroviral therapy before their

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Summary points

- HIV testing is the gateway to both HIV treatment and HIV prevention
- Patients with a diagnosis of HIV infection before moderate to severe immunosuppression occurs should plan for a normal life expectancy with effective access to antiretroviral therapy
- The UK HIV epidemic continues to grow and remains marred by a high proportion of cases (50%) diagnosed at a late stage in the clinical course of the infection, and a persistent undiagnosed fraction (22% of patients living with HIV are unaware of their status)
- Every clinician can, and should, offer patients an HIV test in line with national guidelines
- Primary HIV infection should be considered, and an HIV test offered to all patients with a mononucleosis-like illness
- All patients living with HIV infection should be encouraged to disclose their HIV status to other healthcare providers, especially their general practitioner

Sources and selection criteria

We undertook a review of the literature using Medline, Embase, and the Cochrane database of systematic reviews using a variety of search terms relating to HIV testing, HIV epidemiology, and the management of newly diagnosed HIV infection. We also consulted national clinical guidelines from the British HIV Association, the British Association for Sexual Health and HIV, and the National Institute for Health and Care Excellence. We reviewed conference abstracts from national and international conferences in the specialty area from 2006 to the present. Where possible, we cite the highest quality strata of evidence.

CD4 count has fallen below this threshold (although some guidelines promote starting substantially earlier). By this definition, 47% of patients in the UK in 2012 had a late diagnosis.[3] This fraction declined from 58% in 2003. Late diagnosis remains more common among older age groups (>50 years), black and minority ethnic groups, and male heterosexuals. CD4 count at diagnosis is a strong predictor of short term and long term mortality, with patients whose CD4 count is <350 cells/μL being 10 times more likely to die in the first year after diagnosis than those with CD4 counts >350 cells/μL (fig 1⇓).[3]

Reducing the number of cases of undiagnosed and late diagnosed HIV is thus likely to yield individual and public health benefits. The main barrier to HIV treatment in the UK, and also therefore prevention, remains timely diagnosis. Broadening access to HIV testing is a key strategy.

Who should be tested for HIV infection in the UK?

UK national HIV testing guidelines were published in 2008 (box 1).[1] This guidance has since been ratified by the National Institute for Health and Care Excellence and by a parliamentary select committee in 2011.[11 12]

The three strata of the guidelines are designed to normalise, destigmatise, and expand HIV testing. Routine testing is recommended for all patients presenting to any healthcare service if they belong to a higher risk group, have certain medical conditions (known as HIV indicator conditions), or are accessing care in certain clinical and geographical settings (box 1 and fig 2⇓). Routine testing means that the recommendation to test is made to all, as a matter of course.

What conditions should prompt general practitioners to consider testing for HIV?

The UK guidelines are designed to be applicable to primary care, with the recommendation of routine screening for all adults registering for or accessing care in high prevalence areas, plus targeted testing for those in higher risk groups based on demography and risk factors. Regarding diagnostic testing for indicator diseases, relatively few data are currently available on the predictive value of testing in these conditions and identifying HIV infection, but prospective studies are in progress in secondary and primary care settings. A UK retrospective case-control study of 939 cases and 2576 controls accessing primary care did identify that 12 of the 37 non-AIDS indicator conditions were significantly associated with subsequent HIV diagnosis; most strongly were bacterial pneumonia (odds ratio 47.7, 95% confidence interval 5.6 to 404.0), oral candidiasis (29.4, 6.9 to 125.5), and herpes zoster (25.4, 8.4 to 76.1).[13] Signs and symptoms most associated with HIV were weight loss (13.4, 5.0 to 36.0), pyrexia of unknown origin (7.2, 2.8 to 18.7), and diarrhoea (one or two consultations). Notably, 74.2% of HIV cases (n=697) presented with none of the HIV indicator conditions before diagnosis. Thus a combined testing approach is likely to be optimal. Until more data from prospective studies are available, we would recommend the routine offer of an HIV test to all such patients independent of risk factors. Knowledge of risk factors, including the taking of a sexual history may inform this process but should not influence the decision not to test. We would also strongly recommend routine HIV testing in primary care (and emergency departments and medical admissions units) in patients presenting with mononucleosis-like illnesses, given the possibility of primary HIV infection in the differential diagnosis.

Testing in primary HIV infection

Primary HIV infection or seroconversion illness occurs in up to 80% of people with HIV infection, within 2-4 weeks of exposure to the virus. Such individuals frequently present to primary and secondary care settings with a variety of non-specific symptoms (commonly fever, rash, ulceration, myalgia, pharyngitis, and aseptic meningitis; fig 3⇓) that may mimic other acute infections, notably infectious mononucleosis. Relatively few clinical features are specific, but the presence of oral or genital ulceration is suggestive of primary HIV infection.

Diagnosing primary HIV infection presents an important potential opportunity to make an HIV diagnosis early in the clinical course of HIV infection. On a public health level, a major proportion of new HIV infections are probably acquired from patients who are seroconverting, or have recently seroconverted, as a result of behavioural and virological factors that facilitate transmission.[14] Diagnosing primary HIV infection may help reduce onward transmission by alerting patients to their status.[15] There may also be benefit at the individual level from starting antiretroviral therapy in this context in some patients, and antiretroviral therapy may reduce onward transmission.[16]

Box 1 Summary of UK national HIV testing guidelines, 2008[1]

Who can test?

It should be within the competence of any doctor, midwife, nurse, or trained healthcare worker to obtain consent for and to conduct an HIV test

Who should be offered a test?

Universal HIV testing is recommended in all of the following settings:

Genitourinary medicine or sexual health clinics

Antenatal services

Termination of pregnancy services

Drug dependency programmes

Healthcare services for those with a diagnosis of tuberculosis, hepatitis B, hepatitis C, and lymphoma

An HIV test should be considered in the following settings where the prevalence of diagnosed HIV in the local population (primary care trust/local authority) exceeds 2/1000 population (see fig 2)

All men and women registering in general practice

All general medical admissions

HIV testing should be also routinely offered and recommended to all:

Patients presenting for healthcare where HIV, including primary HIV infection, enters the differential diagnosis (table⇓)

Patients with a diagnosis of a sexually transmitted infection

Sexual partners of men and women known to be positive for antibodies to HIV

Men who have disclosed sexual contact with other men

Female sexual contacts of men who have sex with men

Patients reporting a history of injecting drug use

Men and women known to be from a country of high HIV prevalence (>1%)*

Men and women who report sexual contact abroad or in the UK with people from countries of high HIV prevalence

*Data available at www.unaids.org

The most important predictor of primary HIV infection being diagnosed is suspicion by the patient or clinician.[17 18] All clinicians should make a risk assessment by taking a sexual/HIV exposure history in patients presenting with mononucleosis-like syndromes. Men reporting sex with men should be considered at higher risk, in particular. A fourth generation test should be requested, which is likely to be positive for p24 antigen (a virally derived protein of early infection, the presence of which is detected by fourth generation HIV tests, see fig 4) depending on the duration of the illness. If the test result is negative and clinical suspicion is high, then a repeat test should be performed one or two weeks later. Alternatively, the patient could be referred to specialist services where testing for HIV viral load may be considered.

Who can test?

Any doctor, nurse, midwife, or other trained healthcare provider can offer an HIV test. A lengthy pretest discussion is not necessary. Obtaining consent from a patient for an HIV test should follow the same procedure as that for any other medical investigation. Briefly, it is essential that the patient is made aware of the benefits of accepting an HIV test, the meaning of various test results, and how they will obtain their result and from whom.

If patients decline a test, the reasons why they have made that choice should be explored to ensure that these are not due to incorrect beliefs about the virus or the consequences of testing. If concerns about insurance are a disincentive to testing, this should be challenged. The code of practice from the Association of British Insurers has clearly stated since 1994 that questions about whether anyone has ever had an HIV test or a negative test result should not be asked. Applicants should, however, declare any positive test results (as applies to any other condition).

The outcome of the pretest discussion should be recorded in the case notes. Written consent is not required. In the UK, there is no specific guidance from the General Medical Council relating to consent for infectious diseases—this was repealed in 2006. Testing for HIV should fall within generic good medical practice for obtaining consent as outlined in the GMC guidance document "Consent: patients and doctors making decisions together."

Which HIV test should be used?

Two methods are routinely used to test for HIV: a laboratory based screening assay on a blood sample obtained by venepuncture, or a rapid point of care test. The recommended laboratory based screening assay is one that tests for HIV antibody and p24 antigen simultaneously (p24 antigen is a virally derived protein detectable in the early stages of HIV infection). Such tests are termed fourth generation assays. The "window period" (the time after exposure to HIV before which the antigen or antibody can be reliably detected) is shorter than for older antibody only assays, meaning that most patients will test positive within four weeks of exposure. HIV RNA quantitative assays (viral load tests) are not recommended for screening because of the possibility of false positive results. They also offer only a marginal advantage over fourth generation assays for detecting primary infection (fig 4⇓). Samples that are "reactive" on the screening assay will then be confirmed using a total of three independent assays. These assays should be able to distinguish between HIV-1 and HIV-2 and between HIV antibodies and antigen. A test result positive for antibodies to HIV should only be issued once the serological pattern is confirmed on a second blood sample. Indeterminate results do occur, and patients should be referred to specialist services for discussion and further testing.

Point of care tests yield a "near patient" result within 30 seconds to 30 minutes. Biological samples usually comprise capillary blood ("finger prick") or oral fluid (saliva). Most tests only detect anti-HIV antibodies, and the manufacturer stated window period is usually 6-12 weeks. All commercially available tests have reasonable specificities, but this is always lower than with fourth generation assays: screening in lower prevalence settings

may reduce the positive predictive value of these tests. All reactive point of care results must be confirmed with standard serological tests.

How should patients obtain their results?

A mechanism needs to be in place for patients to obtain their results in a timely fashion, with explicit guidance for those with non-negative test results. Patients who are HIV negative could obtain their test results in several ways: telephone, email, or short message service.

For specific patient populations it may be preferable to deliver the result directly to the patient: all patients with a non-negative result, inpatients, vulnerable patients or those with mental health problems or anxiety, and patients where English is not their first language.

Ensuring safe governance of results

A clear mechanism must be established to ensure that all results—negative and non-negative—are appropriately acted on. This may be facilitated by working collaboratively with pathology or specialist services, but the ultimate responsibility for following up test results rests with the ordering clinician.

Ensuring appropriate transfer to care, and collaborative working with specialist services

Many successful testing ventures involve collaborative working with local specialist services (for example, sexual health/genitourinary medicine, infectious diseases, virology). Specialty services may provide training, facilitate results governance, and develop pathways to specialist care with the test provider. A clear pathway should be developed for the management of patients with reactive or positive results, perhaps involving expedited appointments with specialist physicians, nurses, or sexual health advisers. Patients may also be directed to online information resources and third sector providers.

How often should a patient be offered an HIV test?

How often patients are offered an HIV test will depend on the indication for the test. For opportunistic screening this depends on the patient's level of ongoing risk. Guidance from Public Health England and the British Association for Sexual Health and HIV recommends that men who have sex with men have an HIV test annually, and three monthly if they have sex with new and casual partners; and that black African men and women have an HIV test if they have unprotected sex with new or casual partners.[3] It may be prudent to refer patients at ongoing risk of HIV infection to sexual health services. For indicator disease based testing, a single test should be sufficient to rule out HIV infection, with the exception of testing in patients with suspected primary HIV infection where consideration needs to be given to testing outside of the window period.

Management of patients with newly diagnosed HIV

How do I deal with a "reactive" HIV test result?

The full initial assessment of a patient with newly diagnosed HIV infection is likely to be undertaken in specialist care. However, an increasing number of non-specialist primary and secondary care clinicians will deliver and manage "reactive" HIV test results and deal with the need for immediate patient education and management. It is essential that robust pathways are developed between testing venues and specialist care centres. The clinical context is clearly important, as is the original indication for the HIV test, which will dictate the urgency of referral to specialist care.

The clinician delivering the result should be able to present the following points of information to patients:

The meaning of a reactive screening test and the process of confirming the result—Patients should be advised that a reactive screening test result is a "non-negative" outcome. They should be told that false reactive results do occur and that further tests are needed to verify whether this means that they are positive for antibodies to HIV.

The clinical course of HIV infection: acquisition/transmission, how HIV causes disease, the clinical trajectory of untreated HIV infection—Consider telling patients that HIV is a virus transmitted from human to human primarily through sexual contact or by sharing injecting equipment. Explain that the virus attacks the immune system over many years, which can leave the body vulnerable to serious infections or cancers.

Modern HIV treatment in general terms: availability of antiretroviral therapy, indications for treatment, excellent prognosis—Explain that you will refer the patient to a specialist clinic. Tell him or her that HIV remains incurable, but that excellent and safe treatments are now available that can keep them fit and well. Mention that people living with HIV today should expect to live a long and healthy life with access to treatment.

An initial assessment ought also to be made about the immediate risk of HIV infection to others:

Is a sexual partner at risk of infection?—If sexual exposure has occurred within the preceding 72 hours, consider urgent evaluation and provision of post-exposure prophylaxis if appropriate. Condom use should be discussed and strongly recommended.

Patients with reactive HIV screening test results: how do I know if this is a true positive result?

An initial non-negative screening test result is defined as a "reactive" result. A positive result can only be issued once a second confirmatory test, undertaken on a separate sample, has been obtained. Patients with a reactive screening test result should be advised of this, taking into account the risk factors and clinical context. A reactive test result in the context of a patient admitted with possible *Pneumocystis jiroveci* pneumonia clearly carries a greater value than, for example, a reactive test result in a low risk patient screened as a new registrant to general practice in a high prevalence area. The second sample will confirm or refute the diagnosis and will differentiate between HIV-1 and HIV-2 infection. Close liaison with the laboratory may be required in the context of indeterminate or non-specific results, and referral to specialist care could also be considered.

What is the best way to deliver a positive test result?

A reactive or confirmed positive test result should ideally be delivered face to face by the team or clinician who tested the

patient, in a confidential environment and using clear language (aided by an interpreter if necessary). The result should not be shared with third parties unless explicit consent has been given. Small qualitative studies exploring the psychological impact and engagement in care for those with newly diagnosed HIV infection support this face to face approach.[20-22] Timely access to specialist multidisciplinary care (for example, sexual health advisers) is beneficial.

All patients with newly diagnosed HIV infection should be seen by a specialist HIV clinician within two weeks; sooner if they have HIV attributable symptoms or other acute needs.[1]

What happens at a first consultation with an HIV specialist?

The first consultation provides an opportunity to perform a thorough medical, psychological, and social review, to educate the patient about the clinical course and treatment of HIV, and to request the investigations that will form the basis of future monitoring of the disease.

The medical history

A detailed medical, psychological, and social history should be performed at baseline. A thorough systems review may guide the physical examination and further investigations.

Mental health problems are a risk factor for HIV infection, and depression and anxiety are common in patients living with HIV. UK guidelines recommend screening with questions such as "During the last month, have you often been bothered by feeling down, depressed, or hopeless?"[23]

A sexual history and drug use history should be undertaken to identify the risk of HIV acquisition and partners at risk. These discussions inform partner notification processes and provide an opportunity to discuss evidence based interventions to reduce transmission to susceptible partners (such as condom use, post-exposure prophylaxis, and the use of antiretroviral therapy as a prevention tool). A full sexual health screen should be performed, as sexually transmitted infections facilitate HIV transmission (and acquisition),[24] and co-infection is common. Surveillance data show that 19% of all people with newly diagnosed HIV infection in 2012 were co-diagnosed as having an acute sexually transmitted infection (29% in men who have sex with men).[3] Advice on safer sex should be revisited, and all patients must be counselled on the legal aspects of HIV transmission and disclosure, including "reckless transmission."[25]

Women living with HIV should have a gynaecological and obstetric history taken, and future requirements for pregnancy or contraception should be discussed. All women should have annual cytology, as cytological abnormalities and invasive cervical cancer are more prevalent in women living with HIV, although this is related to the degree of immunosuppression, and antiretroviral therapy is likely to reduce this risk.[26] Patients living with HIV infection, especially men who have sex with men, are also at increased risk of anal cancer, despite antiretroviral therapy.[27] Anal cytology is sensitive at detecting anal dysplasia but lacks specificity,[28] and it remains uncertain whether screening with cytology or high resolution anoscopy is cost effective.[29] UK guidelines do not currently recommend routine screening for anal cancer, but this may be revised in the light of new evidence.[23]

Physical examination

A full physical examination should be undertaken, with particular emphasis on the reticuloendothelial system, skin, and mucous membranes. The extent of examination will also be dictated by the degree of immunosuppression. For example, dilated fundoscopy should be performed in all patients with a confirmed CD4 count <50 cells/μL to exclude cytomegalovirus retinitis.

Baseline investigations

Several baseline investigations are performed (box 2).

The absolute CD4 count is the most useful single surrogate marker of HIV stage and progression.[23] In patients with untreated HIV infection, the likelihood of developing an AIDS defining condition increases exponentially as the CD4 count decreases, particularly with a count of <200 cells/μL.[10] In one study, compared with patients starting highly active antiretroviral therapy with a CD4 count of <50 cells/μL, adjusted hazard ratios for progression to AIDS or death over three years in higher CD4 count groups were 0.74 for 50-99 cells/μL, 0.52 for 100-199 cells/μL, 0.24 for 200-349 cells/μL, and 0.18 for ≥350 cells/μL.[30] Primary HIV infection is associated with a high plasma viral load.[31] This declines substantially 3-6 months after infection to a nearly steady level "set point." It is predominately used to monitor response to antiretroviral therapy. Other tests are also carried out to look for evidence of related liver, kidney, and cardiovascular disease.

Interventions in the initial assessment

Beyond a comprehensive clinical assessment and patient education on the clinical course and treatment of HIV infection, including the excellent prognosis, other things to be discussed may include initiation of partner notification; general advice on health—maintaining a healthy lifestyle, support for smoking cessation, exercise, and nutrition; the increased risk of many comorbidities; social and occupational considerations, with referral to occupational health services if indicated; and provision of immunisation.

Partner notification

Partner notification is the process of informing the sexual partners of someone with a diagnosis of a sexually transmitted infection of their risk of exposure, and of facilitating their evaluation and treatment. An individual may wish to defer disclosure to partners, and some delay may be acceptable if there is no ongoing risk. Attempts to encourage and support disclosure and testing of contacts should be revisited regularly. Some patients will already have a partner known to be HIV positive, but in many cases elicited contacts will require testing. Relatively few prospective trials have been undertaken comparing the effectiveness of different methods of partner notification about HIV, but all reported strategies have high rates of case finding.[32] A recent national audit in the UK showed that among contacts who underwent testing, 21% were subsequently diagnosed as having HIV infection[33]—this figure compares to approximately 3% in men who have sex with men attending genitourinary services[3] and strongly supports the value of partner notification in effectively detecting undiagnosed HIV infection.

Immunisation

Influenza vaccination should be provided annually, and vaccination with the 23 valent pneumococcal vaccine is recommended every 5-10 years. Those who are non-immune to hepatitis A, hepatitis B, measles, and varicella should all be vaccinated (plus rubella in women of childbearing potential).

Box 2 Baseline investigations at first specialist assessment of a patient with newly diagnosed HIV by categories

HIV markers

CD4 T cell count (absolute and percentage); HIV viral load (repeat to confirm baseline in 1-3 months); HIV genotypic drug resistance test; determination of HIV-1 subtype

Biochemistry

Renal function (and calculated estimated glomerular filtration rate by modification of diet in renal disease); liver function tests (bilirubin, alanine transaminase, aspartate transaminase, albumin, γ-glutamyl transferase); bone profile (corrected calcium, phosphate, alkaline phosphatase)

Haematology

Full blood count

Urinalysis

Dipstick test for blood, protein, glucose; urine protein:creatinine ratio

Metabolic assessment

Lipid profile and glucose (cholesterol, high density lipoprotein cholesterol:cholesterol ratio, triglycerides; repeat fasted if random measures above reference ranges)

Serology

Syphilis; hepatitis A (total or IgG); hepatitis B surface antigen, core antibody, surface antibody; hepatitis C antibody (followed by hepatitis C RNA polymerase chain reaction if antibody detected); toxoplasma serology (if CD4 count <200 cells/μL); measles IgG; varicella IgG (unless patient gives reliable history of chickenpox or herpes zoster); rubella IgG in women of childbearing age; schistosoma serology (if >1 month spent in sub-Saharan Africa)

Tuberculosis screening

Interferon γ releasing assay recommended to screen for latent infection (decision to screen depends on country of origin, CD4 count, and time already spent receiving antiretroviral therapy)

Stool sample

Ova, cysts, and parasites (if from, or spent >1 month in, tropics)

Imaging

Chest radiography not recommended routinely unless: signs and symptoms of current or previous chest disease, history of injecting drug use, risk of tuberculosis

Additional

Sexual health screen, cervical cytology in females, cardiovascular risk assessment (for example, Joint British Societies' guidelines on cardiovascular disease; QRISK), fracture risk assessment in those aged >50

Some live vaccines are contraindicated or limited by CD4 count (see the British HIV Association immunisation guidelines[34]).

How can patients be encouraged to disclose their HIV status to other healthcare professionals?

Many patients historically have sought all of their medical care through their HIV centre. However, increasingly general practitioners are responsible for many aspects of the medical care of patients who have HIV. Most patients consent to disclosure of HIV status to their general practitioners. The benefits of increased and enhanced primary care involvement include:

- improved access to and coordination of care
- enhanced management of comorbidities and risk reduction
- experience in managing mental health problems
- experience in managing an aging population
- avoidance of drug-drug interactions
- appropriate management of unrelated medical problems.

It is important that regular, effective, two way communication between the HIV centre and primary care is established. Such communication will help establish a comprehensive list of prescribed drugs, highlight and safely manage important potential drug interactions, and recommend appropriate health screening (for example, cardiovascular disease risk assessment and cervical cytology), which takes account of differences in protocol resulting from differences in HIV status or antiretroviral therapy.

When will my patient start antiretroviral therapy?

A full review of current indications to start antiretroviral therapy is beyond the scope of this review, but box 3 summarises the current 2012 British HIV Association guidelines.[35] Antiretroviral therapy is recommended before the CD4 count is <350 cells/μL, in all AIDS defining illnesses (irrespective of CD4 count), in the context of HIV related comorbidity (including HIV associated nephropathy, idiopathic thrombocytopenic purpura, symptomatic HIV associated neurocognitive disorders, irrespective of CD4 count) and in co-infection with hepatitis B or C virus if the CD4 count is <500 cells/μL. Antiretroviral therapy should also be recommended for non-AIDS defining malignancies requiring immunosuppressive chemotherapy or radiotherapy. Antiretroviral therapy is also indicated during primary HIV infection in specific circumstances.

Figure 3 was provided courtesy of David Hawkins and Medical Illustrations Department, Chelsea and Westminster Hospital, London, UK.

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Box 3 Current indications for starting antiretroviral therapy in the UK[35]

Chronic HIV infection

Patients meeting any of the following criteria should start antiretroviral therapy:

- CD4 count <350 cells/μL
- AIDS defining illness, irrespective of CD4 count
- HIV related comorbidity, including HIV associated nephropathy, idiopathic thrombocytopenic purpura, symptomatic HIV associated neurocognitive disorders, irrespective of CD4 count
- Co-infection with hepatitis B or hepatitis C virus if the CD4 count is <500 cells/μL
- Non-AIDS defining malignancies requiring immunosuppressive chemotherapy or radiotherapy

Patients presenting with AIDS or a major bacterial infection

Patients presenting with an AIDS defining infection or with a serious bacterial infection and CD4 count <200 cells/μL should start antiretroviral therapy within two weeks

Primary HIV infection

Patients with primary HIV infection meeting any of the following criteria should start antiretroviral therapy

- Neurological involvement
- Any AIDS defining illness
- Confirmed CD4 count <350 cells/μL

Treatment to reduce HIV transmission

It is recommended that the evidence showing treatment with antiretroviral therapy lowers the risk of transmission if discussed with all patients, and an assessment of the current risk of transmission to others is made at the time of this discussion. If a patient with a CD4 count >350 cells/μL then wishes to start antiretroviral therapy to reduce the risk of transmission to partners, this decision should be respected and antiretroviral therapy started

Adapted from the British HIV Association guidelines for treatment of HIV-1 positive adults with antiretroviral therapy 2012 (updated November 2013)

Questions for future research

Can we use routine surveillance data to measure the effectiveness of wider HIV testing?

How can we assess the effectiveness and the sustainability of routine and diagnostic testing across the breadth of settings proposed in the testing guidelines?

What about other strategies to diagnose HIV infection, such as home testing?

Additional educational resources

Resources for healthcare professionals

British HIV Association HIV testing guidelines (www.bhiva.org/HIVTesting2008.aspx)—freely accessible; national guidance document

Public Health England HIV/STI surveillance (www.hpa.org.uk/Publications/InfectiousDiseases/HIVAndSTIs/)—freely accessible; national surveillance data on HIV and sexually transmitted infections plus recommendations and policy documents, updated regularly

National AIDS Trust prevention and testing policy documents (www.nat.org.uk/Information-and-Resources/New%20publications.aspx#preventionandtesting)—freely accessible; advocacy and policy documents from the National AIDS Trust

HIV in Europe, HIV indicator conditions: guidance for implementing HIV testing in adults in healthcare settings (www.hiveurope.eu/LinkClick.aspx?fileticket=b8rDoBh8NjM=&tabid=37)—freely accessible; guidance for the implementation of routine HIV testing in indicator conditions across European healthcare settings

Resources for patients

National AIDS Trust: information for patients (www.nat.org.uk/HIV-Facts.aspx)—freely accessible; patient centred resources on all aspects of HIV testing, prevention, and specialist care

Terrence Higgins Trust "My HIV" resource (www.tht.org.uk/myhiv)—freely accessible; self management and information for patients living with HIV

Positively UK, resources for patients (http://positivelyuk.org/)—freely accessible; patient focused resources and stories for patients living with HIV, and their partners

NHS Choices, HIV testing (www.nhs.uk/Conditions/HIV/Pages/Diagnosispg.aspx)—freely accessible; guidance for patients on how and why to access HIV testing in the National Health Service

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Patient consent: Obtained.

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Table

Table 1| List of HIV indicator conditions

Body system/specialty	AIDS defining conditions	Other conditions where HIV testing should be routinely offered
Respiratory	Tuberculosis, pneumocystis	Bacterial pneumonia, aspergillosis
Neurology	Cerebral toxoplasmosis, primary cerebral lymphoma, cryptococcal meningitis, progressive multifocal leucoencephalopathy	Aseptic meningitis/encephalitis, cerebral abscess, space occupying lesion of unknown cause, Guillain-Barré syndrome, transverse myelitis, peripheral neuropathy, dementia, leucoencephalopathy
Dermatology	Kaposi's sarcoma	Severe or recalcitrant seborrhoeic dermatitis, severe or recalcitrant psoriasis, multidermatomal or recurrent herpes zoster
Gastroenterology	Persistent cryptosporidiosis	Oral candidiasis; oral hairy leukoplakia; chronic diarrhoea of unknown cause; weight loss of unknown cause; salmonella, shigella, or campylobacter enteritis; hepatitis B infection; hepatitis C infection
Oncology	Non-Hodgkin's lymphoma	Anal cancer or anal intraepithelial dysplasia, lung cancer, seminoma, head and neck cancer, Hodgkin's lymphoma, Castleman's disease
Gynaecology	Cervical cancer	Vaginal intraepithelial neoplasia, cervical intraepithelial neoplasia grade II or more
Haematology		Any unexplained blood dyscrasia including: thrombocytopenia, neutropenia, lymphopenia
Ophthalmology	Cytomegalovirus retinitis	Infective retinal diseases including herpesviruses and toxoplasma, any unexplained retinopathy
Ear, nose, and throat		Lymphadenopathy of unknown cause, chronic parotitis, lymphoepithelial parotid cysts
Other		Mononucleosis-like syndrome (primary HIV infection), pyrexia of unknown origin, any lymphadenopathy of unknown cause, any sexually transmitted infection

Figures

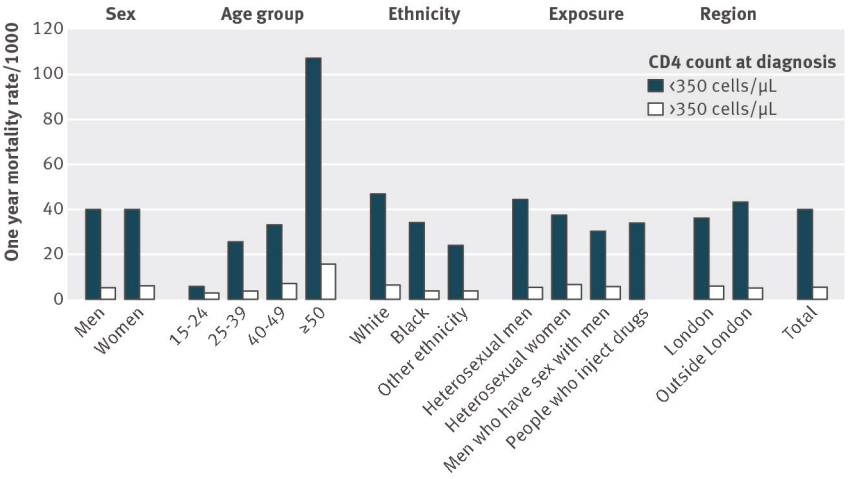

Fig 1 One year mortality (per 1000 population) by CD4 count in people with newly diagnosed HIV, 2010. Adapted from Public Health England. HIV in the United Kingdom, 2013 report[3]

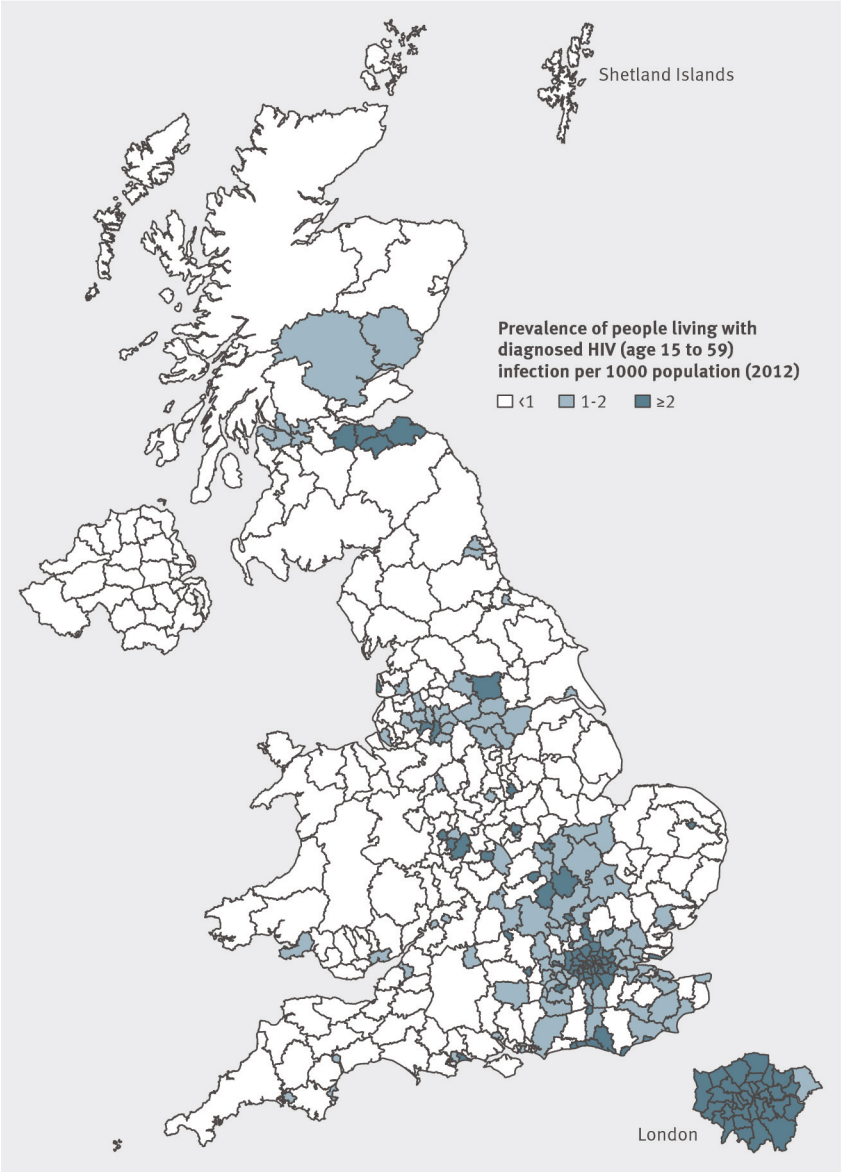

Fig 2 Routine HIV testing in high prevalence areas: prevalence of diagnosed HIV infection by area of residence in population aged 15-59 years, 2012. In areas of high prevalence of diagnosed HIV infection UK national guidelines recommend expanding HIV testing among people admitted to hospital and new registrants to general practice. In 2012, 64 of 326 (20%) local authorities had a diagnosed prevalence above the ≥2/1000 threshold. All but one of the 33 London local authorities had a prevalence above this threshold. Outside London, the five local authorities with the highest prevalence and which were above ≥2/1000 were Brighton and Hove, Salford, Manchester, Blackpool, and Luton. Adapted from Public Health England. HIV in the United Kingdom, 2013 report[3]

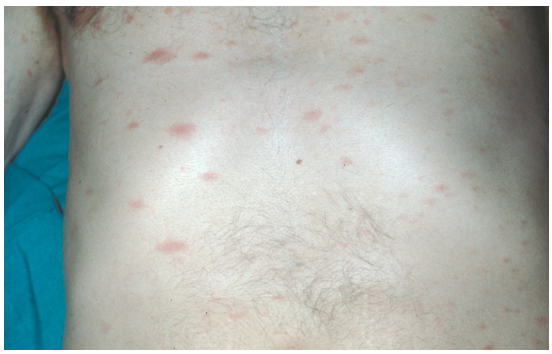

Fig 3 Maculopapular rash of primary HIV infection

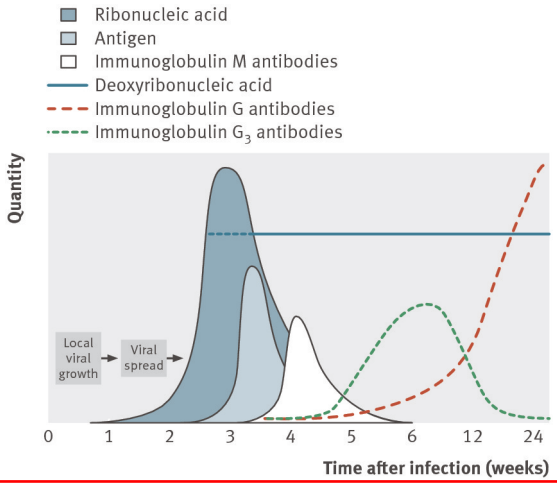

Fig 4 Typical evolution of viral and serological markers after exposure to HIV. Viral markers: RNA=ribonucleic acid; DNA=deoxyribonucleic acid; Ag=antigen. Immunological markers: IgM=immunoglobulin M antibodies; IgG=immunoglobulin G antibodies. Adapted from Murphy and Parry[19]