



Public Health  
England

# **Addressing Late HIV Diagnosis through Screening and Testing: An Evidence Summary**

## About Public Health England

Public Health England's mission is to protect and improve the nation's health and to address inequalities through working with national and local government, the NHS, industry and the voluntary and community sector. PHE is an operationally autonomous executive agency of the Department of Health.

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# Executive summary

## **Purpose**

This document summarises the rationale and evidence for increasing HIV screening and testing in order to support public health and sexual health professionals, including Directors of Public Health, elected members, commissioners and providers, to establish and improve HIV screening and testing in medical and community services.

## **Background**

In 2012, an estimated 21,900 HIV positive people were unaware of their infection, the equivalent of 1 in 5 people living with HIV in the UK. In 2012, 6,360 people were newly diagnosed with HIV, and the largest number were among men who have sex with men (3,250) and heterosexual men and women (2,880). Infections acquired through other routes of transmission remain small.

## **Late diagnosis**

Of the 6,360 new HIV diagnoses made in 2012, 47% (2,990) were diagnosed late (after the point which treatment should have been initiated; <350 CD4 cells/ $\mu$ l blood). A late HIV diagnosis often results from missed opportunities for earlier diagnosis, and can have adverse consequences on:

- the individual; as life expectancy is near-normal and clinical outcomes improved if HIV is diagnosed and treated promptly
- public health; as diagnosis can reduce onward transmission with treatment and support for behaviour change
- costs of HIV treatment and care; which are lower in individuals diagnosed earlier

## **HIV screening and testing**

Expansion of HIV screening and testing is a critical response to the challenge of controlling the HIV epidemic and reducing late HIV diagnosis. Programmes to increase HIV testing have been shown to be effective, cost-effective and provide a positive return on investment.

Commissioning of HIV screening and testing falls to local authorities, clinical commissioning groups and NHS England. The Public Health Outcomes Framework (PHOF) has included the proportion of persons presenting with HIV at a late stage of infection as a high level indicator of essential actions to be taken to protect the public's health.

National HIV testing guidelines, endorsed by the National Institute of Health and Care Excellence (NICE), recommend HIV testing of all patients attending specified services, presenting with an indicator condition or reporting a history of high risk behaviour. Furthermore, they recommend that HIV screening and testing be expanded into general medical services (e.g. hospital general medical admissions) in areas of high HIV prevalence (where the local diagnosed HIV prevalence  $\geq 2$  per 1,000 16-59 year olds).

Nationally, HIV screening and testing coverage among attendees of genitourinary medicine (GUM), antenatal services, needle exchange and other drug services is high. Low levels of HIV screening and testing among patients with indicator conditions or attending termination of pregnancy services, hospital general medical admissions, and primary care have been reported, even though screening in these services has been shown to be feasible, acceptable, effective and cost-effective.

Testing in non-medical settings such as community HIV testing, self-sampling and self-testing for HIV broadens the options available to people wishing to take an HIV test. Although testing in community settings has often exceeded cost-effectiveness thresholds, data to ascertain if testing in the community was more effective than in traditional settings were inconclusive. Initial evaluations of self-sampling for HIV report high uptake and new diagnoses, and data on self-testing for HIV will follow the repeal of the ban of self-testing kit sales on 6<sup>th</sup> April 2014.

### **Monitoring and Evaluation**

The monitoring and evaluation of HIV testing in some medical services (e.g. GUM and antenatal services) is reported in a routine and regular manner. Robust monitoring and evaluation should be implemented where interventions seek either to establish or improve HIV testing, especially in those settings where there is a lack of evidence as to the best model (e.g. primary care), or where new technologies are to be established (e.g. employing point of care testing, HIV self-testing).

## List of Abbreviations

AGM	Acute general medicine
BASHH	British Association for Sexual Health and HIV
BHIVA	British HIV Association
cART	Combination antiretroviral therapy
GP	General practitioner
GUM	Genitourinary medicine
HIV	Human immunodeficiency virus
MSM	Men who have sex with men
NATSAL	National Surveys of Sexual Attitudes and Lifestyles
NICE	National Institute for Health and Care Excellence
PHOF	Public Health Outcomes Framework
POCT	Point of care test
PPV	Positive predictive value
STI	Sexually transmitted infection
TAsP	Treatment as prevention
TB	Tuberculosis
TOP	Termination of pregnancy

## Scope and Procedure

### Computerised literature search

A computerised literature search of Medline was performed using PubMed ([www.pubmed.org](http://www.pubmed.org)). Key terms were used to search titles and abstracts. Evidence was included from publications dated 2000 to 2014. Wherever available, research from the UK is cited and prioritised. Evidence from other developed countries (i.e. United States of America, Europe and Australia) is included if no or limited evidence was available from the UK, and where the setting was comparable and relevant to the UK health care system.

### Grading of evidence

Evidence was graded according to criteria developed by the US Department of Health and Human Services' Agency for Healthcare Policy and Research for grading scientific evidence, now known as the Agency for Healthcare Research and Quality (see Appendix 1 for grading criteria).

# Introduction

## Aims and Objectives

The aim of this document is to summarise the evidence available around Human immunodeficiency virus (HIV) screening and testing in different medical, community and justice services. It has sought to ascertain the feasibility, acceptability, effectiveness and cost-effectiveness, of increased provision of screening and testing in these different settings, and how this will address late HIV diagnosis.

The main objectives are to summarise available evidence for:

1. The rationale for increasing HIV screening and testing;
2. Current best estimates for cost-effectiveness and return on investment for HIV screening and testing;
3. HIV screening and testing policies both in different settings (i.e. medical, community and justice) and for different medical conditions.

This document is intended as a resource for use by public health and sexual health professionals, including Directors of Public Health, elected members, commissioners and providers of HIV screening and testing services.

This document has not included an evidence summary of HIV screening and testing in specific most at-risk communities, but rather has focussed on these policies in reference to services (whether health, community or justice). Similarly, this document has not included evidence for the mandatory HIV screening of blood and organ donations.

## Background

### HIV epidemiology in the UK

In 2012 there were an estimated 98,400 (95% credible interval 93,500 – 104,300) people living with HIV in the UK, representing an overall prevalence of 1.5 per 1,000 population (1.0 in women and 2.1 in men). Of this total, an estimated 21,900 (1 in 5) were unaware of their HIV positive status, and this number of undiagnosed people has remained relatively constant over recent years [1].

There were 6,360 new HIV diagnoses made in the UK in 2012; representing a diagnosis rate of 1.0 per 10,000 population. Of these 6,360 new diagnoses, 47%

(2,990) were diagnosed late (a point after treatment should have been initiated; <350 CD4 cells/ $\mu$ l blood), and 28% (1,770) were severely immunocompromised (<200 CD4 cells/ $\mu$ l blood). Late diagnosis of HIV is the most important predictor of morbidity and one-year mortality.

Most HIV transmission in the UK occurs through sexual contact (both between people of the same and opposite sex); the two groups at highest risk of HIV infection are men who have sex with men (MSM) and the black African heterosexual population. The number of infections acquired through other routes of transmission (i.e. injecting drug use, nosocomial infection and mother-to-child-transmission) remain relatively small.

### Men who have sex with men

In 2012, an estimated 40,900 MSM were living with HIV, representing an overall prevalence of nearly one in 20 (47 per 1,000). This prevalence was higher among MSM living in London (80 per 1,000) than elsewhere in the UK (29 per 1,000). Nearly one in five MSM (17%; 7,300) living with HIV were unaware of their status. In 2012, 51% (3,250) of new diagnoses were among MSM; the highest number ever reported in the UK, and may be explained by an increase in HIV testing (up 13% in sexual health services in England), as well as a continued high rate of transmission. Of the newly diagnosed MSM in 2012, 34% were diagnosed at a late-stage of infection [1].

### Black African population

In 2012, an estimated 31,800 black African men and women (11,100 men and 20,700 women) were living with HIV in the UK, representing an overall prevalence of 26 per 1,000 for African-born men and 51 per 1,000 for African-born women, of which 27% of men (3,000) and 21% of women (4,300) were undiagnosed. Of the 1,522 black Africans (625 men and 897 women) newly diagnosed with HIV In 2012, 66% of men and 61% of women were diagnosed at a late-stage of infection [1].

### Adverse consequences of late HIV diagnosis

A late HIV diagnosis can have adverse consequences on the individual, public health, and costs of HIV treatment and care.

### Impact on the individual

If an HIV infection is diagnosed promptly (which is facilitated by expanded HIV testing), and treatment with combination antiretroviral therapy (cART) is initiated and maintained, then people living with HIV can expect a near normal lifespan, better clinical outcomes and improved quality of life [2] **Evidence level IIb**; [3, 4]

### Mathematical models.



## Impact on public health

A diagnosis of HIV can reduce onward transmission through treatment and changes in behaviour. Antiretroviral treatment with successfully suppressive cART can be used as prevention (treatment as prevention; TAsP), lowering the viral load and therefore the probability of transmission [5] **Evidence level Ib**. Individuals diagnosed with HIV infection have also demonstrated a reduction in risk behaviour [6] **Evidence level IIb**, which in the USA has been shown to contribute to a reduced rate of onward transmission [7] **Evidence level Ia**.

## Costs of late HIV diagnosis

Earlier diagnosis of HIV is cheaper than late diagnosis, as earlier diagnosis and treatment leads to less late-stage disease comorbidities, and consequently a reduced requirement for inpatient care. In the UK, data from 1996 to 2008 showed that the annual estimated cost for starting standard first line anti-retroviral therapy was £12,812 for HIV positive individuals who were severely immunocompromised (CD4 count <200 cells/ $\mu$ l blood), but 18% less (£10,478) if treatment was initiated at CD4 count >200 cells/ $\mu$ l blood [8] **Evidence level III**.

Similarly, in Canada, costs of treating comorbidities associated with a late HIV diagnosis were also high, including inpatient care and non-HIV drug costs. This short-term increase in costs was accompanied by a long-term increased annual cost of treatment and care in individuals who initiated cART at a later stage of HIV disease progression. This increase was sustained over a 15 year study period, with direct medical costs almost two fold higher in following years for those diagnosed late, compared to those diagnosed at an earlier disease stage. This was the case even though those diagnosed late exhibited treatment-mediated CD4 count recovery; demonstrating the life-long legacy costs of a late diagnosis [9] **Evidence level III**.

## Missed opportunities for earlier HIV diagnosis

In 2008, a survey of newly diagnosed HIV positive black African individuals reported that in the 12 months preceding their diagnosis 76% had presented to health care services and 15% to inpatient services [10] **Evidence level III**. In 2012, an audit performed on behalf of the British HIV Association (BHIVA) found that there had been missed opportunities for an earlier HIV diagnosis in a quarter of newly diagnosed HIV positive individuals [11] **Evidence level III**.

Despite national HIV testing guidelines being released in 2008, adherence to these does not appear to be universal. A meta-analysis of 30 studies revealed that test coverage in settings where HIV testing was recommended reached 27% of eligible individuals (95% CI 22% to 32%). Patient uptake of testing was 72%, whereas provider test offer was lower (40%); indicating that the barrier to increased HIV testing may not

be with patient acceptability, but instead with test providers [12, 13] **Evidence level Ia, IIb.**

## Policy Context

Expansion of HIV screening and testing is a critical response to the challenge of controlling the HIV epidemic and reducing late HIV diagnosis; a high level Public Health Outcomes Framework (PHOF) indicator. Such strategies have also been recommended in guidelines for the USA [14], and in Europe [15].

When compared to the National Survey of Sexual Attitudes and Lifestyles (NATSAL)-2 (1999-2001) survey, NATSAL-3 (2010-2012) reported an increase in the proportion of people having an HIV test in the last 5 years (27.6% of women, and 16.9% of men in 2010-2012, compared to 8.7% women and 9.2% men in 1999-2001) [16]. The proportion of people having an HIV test who had attended specific services, or who were those most at-risk (as defined by national guidelines [17]) also increased [18].

## Policies on HIV screening and testing

National HIV testing guidelines developed by BHIVA and the British Association for Sexual Health and HIV (BASHH) endorsed the routine offer and recommendation of an HIV test to all patients attending specified services (e.g. genitourinary medicine [GUM] clinics), presenting with HIV indicator conditions (Appendix 2), or reporting a history of risk behaviour. Furthermore, the guidelines advocated the expansion of HIV testing in high prevalence areas (where local diagnosed HIV prevalence is  $\geq 2$  per 1,000 resident 15-59 year olds) to include patients admitted to hospital acute general medical (AGM) admissions and adults registering in general practice [17].

The National Institute for Health and Care Excellence (NICE) published guidance in March 2011 for increasing the uptake of HIV testing in black African and MSM communities and endorsed recommendations for HIV testing as outlined in the national guidelines (see above). Furthermore, the guidance called for the development of local strategies to overcome barriers to more widespread testing [19, 20].

## Commissioning framework for HIV screening and testing

Under the Health and Social Care Act, upper tier and unitary local authorities have assumed leadership for public health [21]. As part of this responsibility, local authorities have been mandated to commission comprehensive sexual health services. The Joint Strategic Needs Assessments will assist local authorities to prioritise and monitor progress for this indicator.

Commissioning of HIV screening and testing falls to local authorities, clinical commissioning groups and NHS England. Each body has distinct responsibility for HIV

testing in different settings and these are outlined in [Sexual Health Commissioning Frequently Asked Questions](#).

## Public Health Outcomes Framework Indicator

The Public Health Outcomes Framework, published in January 2012, included a range of outcome indicators against which local public health delivery is to be measured. The Health Protection domain of the Public Health Outcomes Framework has included the proportion of persons presenting with HIV at a late stage of infection (CD4 count <350 cells/ $\mu$ l blood) as an indicator of essential actions to be taken to protect the public's health.

## Effectiveness and economics of HIV screening and testing

### Effectiveness

In the District of Columbia USA, a programme of expanded HIV testing, which included a 4.5 fold increase in HIV testing of the general population over a 5 year period (2005 to 2009), along with an initiative to improve linkage to care, was associated with earlier diagnosis (the median CD4 count at diagnosis increased by 9.5%; from 346 to 379 cells/ $\mu$ l blood), entry into clinical care, and slower disease progression [22] **Evidence level IIa**.

In the UK, the possible impact of increased HIV testing on the HIV epidemic was illustrated by the mathematical modelling of a counterfactual scenario which hypothesised that a 43% increase in HIV testing amongst MSM (from the actual 25% tested/year, to a hypothetical 68%) would lead to a 25% reduction in HIV incidence in this group [23].

### Cost-effectiveness

In the USA, HIV testing was deemed cost-effective if one undiagnosed person was identified per 1,000 tests performed; although this economic modelling did not include secondary savings from reduced onward transmission [24, 25] **Mathematical models**. In France and Portugal it has been estimated that an HIV test undertaken in a lifetime will be cost-effective for the general population, and more frequent testing is economically justifiable in high-risk groups [26, 27] **Mathematical models**.

To date, there are limited data on the cost-effectiveness of expanded HIV testing in the UK. An estimated £762 million was spent in 2010 on HIV treatment and care and the lifetime costs of an HIV infection have been estimated at between £280,000 and £360,000 [28]. NICE have produced a costing tool to estimate the impact of implementing their guidance [29] which estimated:

- a shift of 1% of patients being diagnosed at an earlier stage of disease could produce savings of around £0.22 million a year for MSM, and £0.27 million a year for black Africans, in England
- cost savings from reduced onward transmission in year 1 were estimated as £0.9 million for MSM and £0.3 million for black Africans in England. This effect would be cumulative, with savings increasing year on year
- 3,500 cases of onward transmission would be prevented cumulatively within five years of implementing NICE guidelines, resulting in savings of £18 million in treatment costs per year

### Justification for expanded testing in high prevalence areas

National HIV testing guidelines advocated expanded HIV testing in high prevalence areas where diagnosed HIV infections was  $\geq 2$  per 1,000 resident population. At the time, the ratio of diagnosed to undiagnosed HIV infection was 2:1, and thus establishing expanded testing programmes in those areas would more likely meet the cost-effectiveness diagnosis rate of 1 per 1,000 tests [24, 25]. The definition of a high prevalence area has remained unchanged because:

- although the ratio of diagnosed to undiagnosed HIV positive individuals has changed over time (estimated at 4:1 in 2012), back-calculations indicate that the estimated number of undiagnosed infections (and therefore the prevalence of undiagnosed infection) has remained stable, at least in MSM populations [30]; as newly diagnosed are replaced by incident infections each year
- high prevalence areas not only represent the likelihood of high undiagnosed prevalence, but also a higher proportion of the population belonging to most at-risk groups
- national guidelines recommended opportunistic screening in many medical settings where individuals are likely to have a higher prevalence of undiagnosed HIV due to ill health (i.e. having symptoms resulting from or associated with HIV infection) or belonging to a population at higher risk of HIV infection

### Return on investment

In the USA, the return on investment of a \$102.3 million three year initiative, to expand testing in populations with high prevalence of HIV infection, was calculated at \$1.95 per dollar invested. A positive return on investment resulted when the prevalence of undiagnosed HIV infection was  $\geq 1.2$  per 1,000 population. The programme resulted in 2.7 million persons being tested with a new diagnosis rate of 0.7% (approximately 18,900). Assumed earlier diagnosis of HIV infection as a result of the initiative was estimated to have averted 3,381 new infections [31] **Mathematical model**. No British

study has detailed return on investment, however this American study indicates that a positive return on investment may also be achievable within the UK.

### Frequency of testing

A number of HIV testing policies in the UK have recommended that MSM should have an 'at least annual' HIV test. In addition, Public Health England has recommended that MSM having unprotected sex with new or casual partners should have an HIV test every 3 months, and black African men and women are advised to have an HIV test if having unprotected sex with new or casual partners [1].

There is evidence to support more frequent testing than annually in individuals at high risk of infection. A Scottish study showed significantly less undiagnosed HIV in MSM who had tested for HIV within the past 6 months compared to those who had not [32] **Evidence level III**. Quarterly instead of annual HIV testing among MSM has been shown to have the potential to reduce new infections by 14% over a ten year period in an Australian modelling study [33] **Mathematical model**. Mathematical modelling has also shown that in the USA testing of high-risk MSM at 3 month intervals was cost saving, in terms of new infections averted, compared to an annual testing regime [34].

## Screening & Testing Policies

### Systematic opportunistic HIV screening

#### Antenatal services

The UK National Screening Committee recommends antenatal screening for HIV. A universal offer of an HIV test was initiated in antenatal clinics in 1999, and in 2012 the national uptake of HIV testing among the 675,800 pregnant women attending antenatal services was 98%, where 0.19% (1,310) were HIV positive, and 0.04% were newly diagnosed [1] **Evidence level III**. The proportion of mother-to-child transmission at delivery from diagnosed HIV positive women has also fallen; from around 20% in the early 1990s to 0.5% in 2010/11 [35].

Three London hospitals with specialist HIV antenatal care documented partner notification activity in 145 pregnant HIV positive women attending the services from 2004 to 2006 [36] **Evidence level III**. Forty three percent of partners were tested for HIV infection (62/145), 13% of whom (8/62) were subsequently newly diagnosed as HIV positive. Although partner notification practices enabled new diagnoses of HIV positive people previously unaware of their status, this study also highlighted the consideration that must be taken when implementing partner notification; as 11 HIV

positive women reported relationship breakdown due to HIV infection, and 1 in ten women reported domestic violence.

### Termination of pregnancy services

In an unlinked anonymous study of women attending Termination of Pregnancy (TOP) services at London clinics in 2005, 1% were found to be HIV positive; more than twice the 0.4% prevalence in women giving birth in the same geographical area [37]

#### **Evidence level III.**

A study of testing for HIV in a TOP service in City and Hackney reported a 100% offer of an HIV test, a 60% uptake and a 0.3% (n=7) positivity, compared to 0.1% of women testing HIV positive through antenatal services during the same time period [38]

#### **Evidence level IIb.**

Little information is available on current coverage of HIV testing in TOP services. Current TOP service guidelines recommend a risk assessment for sexually transmitted infections (STI) including HIV among attendees, but not a routine offer of an HIV test [39]. National testing guidelines, endorsed by NICE, recommend routine offer of an HIV test to all women attending TOP services [17].

### General medical admissions in high prevalence areas

Since 2010, six studies have been published examining the feasibility, acceptability and effectiveness of systematic opportunistic screening for HIV in hospital AGM admissions in areas of high diagnosed HIV prevalence (detailed in Appendix 3).

Of the six studies, the median offer rate was 34.4% (range 15.6 to 48.0%); indicating the feasibility of routine HIV testing in these services. The main barriers to routine HIV testing identified by staff in AGM were a requirement for additional training, concerns over suboptimal knowledge of the test provider, potential inadequate patient privacy, and lack of time required to offer and perform testing. Nonetheless, 98% of healthcare staff supported testing in non-traditional settings, and 79% agreed that it should be offered in the AGM department in which they work [13] **Evidence level IIb.**

Acceptability among patients was high and uptake rates ranged from 70 to 88%; suggesting that the main barrier to HIV test expansion appears to be low test offer rate to the eligible population, not patient acceptability.

The positivity reported from the six studies ranged from 1.6 to 22.2 new HIV diagnoses per 1,000 tests, and four studies reported new diagnosis rates higher than the local area diagnosed prevalence. Individuals diagnosed solely due to the expansion of HIV testing, with no clinical indicators of HIV infection, had significantly higher CD4 counts than those presenting with indicators of HIV infection [40] **Evidence level III.** However, in one study, although coverage of HIV testing was 44% of admissions, a parallel

anonymous sero-prevalence study revealed that undiagnosed HIV infections were still missed [41] **Evidence level III**.

The cost-effectiveness threshold of 1 new diagnosis per 1,000 tests was exceeded in all six studies reported here. The more cost-effective option to offer HIV testing within AGM settings was by staff of lower pay bands; who were shown to be capable and willing to provide such a service [13, 40] **Evidence level IIb, IIb**.

Sustainability of expanding testing in AGM admissions was evidenced by one study reporting a continued impact on test coverage after the study had closed; with a significant increase in the number of tests performed in the year following the pilot study [42] **Evidence level III**.

## Prisons

In 2014, the routine offer and recommendation of a test for blood borne viruses (Hepatitis B, Hepatitis C and HIV) will be introduced for all offenders upon reception in prison, which will be repeated according to the individual's risk.

The most recent data (from 1997/8) of HIV prevalence in prisons was collected through unlinked anonymous testing offered in eight prisons. Uptake was 82% (3,930/4,778) among eligible prisoners, and 0.4% (14) were diagnosed with HIV [43] **Evidence level III**. In two studies among female prisoners using prison blood borne virus services, uptake of testing was high (69% and 80% respectively), with one study reporting 0.8% HIV positivity [44], and the other no new HIV diagnoses [45] **Evidence level III**.

## HIV testing of higher risk patient groups

### GUM clinics

In 2012, the coverage of HIV testing among GUM clinic attendees in England was 79%. A recent unlinked anonymous survey of urine samples provided by male attendees, who had not been tested for HIV and were not known to be HIV positive, showed that 0.5% of men were leaving clinics with an undiagnosed, untreated HIV infection [1].

Partner notification offers both clinical benefit to undiagnosed, infected individuals, and also public health benefit to reduce transmission, morbidity and mortality [46]. A report of partner notification taking place at a district general hospital in Watford from 2000 to 2002, detailed that 42% (25/59) of the current partners of newly diagnosed HIV positive people were tested for HIV [47] **Evidence level III**. Sixty percent of those tested (15/25) were subsequently diagnosed as HIV positive. A strategy for expansion of HIV testing to those most at-risk is couples voluntary HIV counselling and testing, which has been reported as acceptable among MSM [48, 49] **Evidence level III**.

## Needle exchange and other drug services

Guidelines for the clinical management of drug users state that all individuals should be offered an HIV test annually, or more frequently if clinical symptoms are suggestive of seroconversion. In 2011, 77% of HIV negative drug users reported that they had ever had a named HIV test [1].

## Patients with indicator conditions

A number of indicator illnesses with high background HIV prevalence are treated in general and specialist medical services. It is currently recommended that all individuals presenting with these conditions, where HIV infection is considered as the differential diagnosis, are offered an HIV test. A list of indicator diseases, along with the estimated prevalence of HIV in each patient population, can be found in Appendix 2.

A review of ten studies (published 2011 to 2013) reporting data on patients presenting with indicator diseases who were subsequently tested for HIV found that, despite national HIV testing guidelines recommending a test for all patients in such settings, only 22% (95% CI: 14 to 31%) of those eligible received a test [12] **Evidence level Ia.** Where data were available, acceptability of testing was high (87%), and in the six studies reporting test result data, 2.7% (range 1.1 to 4.4%) of individuals tested were diagnosed HIV positive. Five of the ten studies were performed in areas of high diagnosed prevalence ( $\geq 2$  per 1000 population), with HIV positivity rates (when reported; n=3) ranging from 1.0 to 11.8%. Furthermore, in areas of low diagnosed HIV prevalence, patients presenting with indicator conditions should be offered a test as positivity rates ranged from 0.0 to 6.7%.

A study performed in Scotland showed a reduction in missed presentations over time, when two cohorts, spanning 6 years each and four years apart, were compared for missed presentations, late diagnosis and time to diagnosis. No improvement was observed in the proportion of late diagnoses. Clinical indicators of infection were missed particularly in older individuals of UK origin from more deprived communities. Forty six percent of missed presentations occurred in general secondary care – highlighting the need for increased testing in non-specialist services [50] **Evidence level III.**

In England and Wales (2005) 7.4% of individuals diagnosed with Tuberculosis (TB) were also HIV positive [51] **Evidence level Ia.** NICE has recommended the screening of migrants from high TB prevalence (incidence TB  $>40$  per 100,000 population) countries for latent TB infection [52]. Pilot programmes to assess feasibility, acceptability and effectiveness of this approach are currently underway. However, as 18 of the 22 countries identified with high TB prevalence also have high HIV prevalence, and screening for latent TB infection also requires an HIV test, this



represents an opportunity to identify previously undiagnosed HIV infection in a population at higher risk of infection.

## HIV testing in other medical settings

### Primary care

Since 2010, only three published studies have examined the feasibility, acceptability and effectiveness of expanded HIV testing in primary care in areas of high diagnosed HIV prevalence [13, 53, 54]. Therefore evidence inclusion criteria were altered to include results of six studies that have been published in reports and conference abstracts (detailed in Appendix 4).

Of the six studies that reported offer rate, the median was 59.0% (range 24.9 to 100.0%); indicating the feasibility of routine HIV testing in these services. A study of General Practitioners' (GP) opinions of HIV testing found that the main reported barrier to performing HIV tests was the perceived lack of patient acceptability. This suggests a discrepancy between the perceptions of the healthcare provider, and the reality of patients' attitudes [55] **Evidence level III.**

Patient acceptability of testing in general practice has been shown to be high; with median testing uptake rates of 50.4% (range 18.4 to 75.4%). Individuals who did not test reported a variety of reasons, however young men reported that testing for HIV was more acceptable in general practice (80%) than GUM (67%) [56] **Evidence level III.** A qualitative study found broad support among patients for the introduction of opt-out HIV testing in general practice, although concerns were raised about informed consent [57] **Evidence level III.**

Forty practices in East London were randomised in a controlled trial of staff training to offer a point of care test (POCT) to all new registrants. The uptake rate of POCT in the intervention arm was 44.5%, and the mean CD4 count at diagnosis was significantly higher in HIV positive individuals attending intervention practices compared to control practices (369 vs 194 cells/ $\mu$ l blood;  $p=0.025$ ) [58] **Evidence level Ib.** Another training intervention for general practice staff saw rates of HIV testing tripled, and new HIV diagnoses doubled [53] **Evidence level IIa.** In south-west London between 2007 and 2011, a 184% increase in new HIV diagnoses in primary care and other non-GUM settings was associated with a primary care education programme and the piloting of the offer of POCT for new registrants. The median CD4 count at diagnosis increased by 30% (from 233 to 304 CD4 cells/ $\mu$ l blood), and the proportion of patients diagnosed when severely immunocompromised (<200 CD4 cells/ $\mu$ l blood) decreased by 24% [54] **Evidence level IIb.** Following the publication of expanded testing guidelines, an audit reported that the proportion of new diagnoses made in general practice doubled from 5% in 2003 to 10% in 2010 [11] **Evidence level III.**

Limited cost-effectiveness evidence on testing in general practice exists. The cost-effectiveness threshold of 1 new diagnosis per 1,000 tests was equalled or exceeded in all but two studies, each of which took place in a single practice and made no new diagnoses over the study period [13] **Evidence level IIb.**

## Testing in non-medical settings

### Community HIV testing

A review identified 44 studies to assess the evidence for feasibility, acceptability and effectiveness of HIV testing in community settings in resource-rich countries. Acceptability of community HIV testing was high among both patients and staff, with evidence that the use of rapid POCT increased the numbers of clients receiving the results of their test compared to when serological (lab based) test methods were used. The majority of studies exceeded the cost-effectiveness threshold of 1 new diagnosis per 1,000 tests. However, data to ascertain if testing in the community was more effective than in traditional clinical settings was not conclusive [59] **Evidence level IIb.**

A study of community outreach testing in Brighton, an area of high diagnosed HIV prevalence, demonstrated that community rapid HIV testing, offered once a week during an evening drop-in session staffed by GUM professionals, was feasible and reached the high-risk target group. MSM tested in this community setting were significantly younger, and less likely to test positive for HIV than those accessing tests through GUM clinics. Individuals diagnosed with HIV showed a trend towards higher CD4 counts, and more recent infection [60] **Evidence level III.**

### Self-sampling for HIV

Self-sampling is the provision of sampling equipment, enabling clients to obtain the required sample themselves (either saliva from an oral swab or blood from a finger prick), and return to the test provider for laboratory processing. The result of the test is communicated to the client through a healthcare worker.

Only two abstracts have been published detailing HIV self-sampling, which both report a high uptake and high positivity [61, 62]. In the six months of operation of two national HIV self-sampling services, nearly 16,000 self-sampling kits were delivered, 9,000 returned, and 170 people newly diagnosed [63] **Evidence level III.**

### Self-testing for HIV

Self-testing involves a client undertaking testing and receiving the result in a single session, away from the medical setting. The UK government has repealed a ban on the sale of HIV self-testing kits, which will come into effect on the 6<sup>th</sup> April 2014.

Feasibility of self-testing has been backed by favourable opinion on instant test results, with increased anonymity, confidentiality and privacy cited as benefits [64] **Evidence level III**. Concerns exist over a potential reduction in linkage to care of those with reactive test results [64] **Evidence level III**, and that lack of post-test counselling may result in adverse psychological events [65, 66] **Evidence level IIb, III**. An unsupervised testing strategy in the USA reported that 96% of individuals who tested positive said they would seek post-test counselling [64] **Evidence level III**.

Acceptability of self-testing is high, and has been shown to be popular among those who have never tested for HIV before; with half of the participants in two Spanish studies described as first-time testers [64, 65] **Evidence level III, IIb**. Nonetheless, two studies in the USA which have reported that between 80% and 97% of participants wanted to use the POCT to test their sexual partners [64] **Evidence level III**. This highlights a potential risk of abuse of HIV self-testing kits to perform tests on others without their informed consent.

Self-testing has been described as “very easy to use” (95% of urban MSM in USA), however evidence suggests that kits can be subject to operator errors in test conduct and interpretation (1% invalid results from finger prick test, and 5.4% interpretation error rate in a Spanish study) [64] **Evidence level III**. Cost-effectiveness of self-testing is yet to be established; however the reduced requirement for healthcare professionals, clinical and laboratory facilities is likely to reduce the cost of testing significantly.

## Monitoring and evaluation

The monitoring and evaluation of HIV testing in some medical services (e.g. GUM and antenatal services) is reported in a routine and regular manner. Robust monitoring and evaluation should be implemented where interventions seek either to establish or improve HIV testing, especially in those settings where there is a lack of evidence as to the best model (e.g. primary care), or where new technologies are to be established (e.g. employing POCT, HIV self-testing). Monitoring of interventions should collect data to ascertain coverage, uptake, positivity, linkage into care of those with a reactive result, test quality and performance (e.g. false positives), and costs [67].

The use of POCT should be closely monitored so that the rate and consequences of false reactive results are comprehensively evaluated, as these tests may not be as specific or sensitive as laboratory fourth generation serological tests. This is especially so if POCT are deployed to offer testing to lower prevalence populations as positive predictive values (PPV) will consequently be lower. A decision regarding the use of POCT should be made at the level of the service, and effective clinical pathways should exist for the rapid confirmation of reactive results.

## Appendix 1

Levels and grading of evidence [68].

<b>Level</b>	<b>Type of evidence</b>
Ia	Evidence from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomisation
IIb	Evidence obtained from at least one well-designed quasi-experimental study
III	Evidence obtained from well-designed, non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

## Appendix 2

Clinical indicator diseases for adult HIV infection, and the reported HIV prevalence within the populations diagnosed with the disease of interest. Adapted from BHIVA testing guidelines 2008, and HIV Indicator Conditions: Guidance for Implementing HIV Testing in Adults in Health Care Settings [17, 69].

Speciality	AIDS-defining conditions	HIV prev., %	Other conditions where HIV testing should be offered	HIV prev., %
<i>Respiratory</i>	Tuberculosis		Bacterial pneumonia	2.4 – 4.0 <sup>16, 17</sup>
	Pneumocystis		Aspergillosis	
<i>Neurology</i>	Cerebral toxoplasmosis		Aseptic meningitis /encephalitis	
	Primary cerebral lymphoma		Cerebral abscess	
	Cryptococcal meningitis		Space occupying lesion of unknown cause	
	Progressive multifocal leucoencephalopathy		Guillain–Barré syndrome	
			Transverse myelitis	
			Peripheral neuropathy	
			Dementia	
		Leucoencephalopathy		
<i>Dermatology</i>	Kaposi's sarcoma		Severe or recalcitrant seborrhoeic dermatitis	2.1 <sup>1</sup>
			Severe or recalcitrant psoriasis	
			Multidermatomal or recurrent herpes zoster	2.9 <sup>1, 8, 9</sup>
<i>Gastro-enterology</i>	Persistent cryptosporidiosis		Oral candidiasis	6.0 – 23.0 <sup>18, 19</sup>
			Oral hairy leukoplakia	
			Chronic diarrhoea of unknown cause	
			Weight loss of unknown cause	
			Salmonella, shigella or campylobacter	
			Hepatitis B infection	0.4 – 5.7 <sup>1, 10</sup>
			Hepatitis C infection	8.6 <sup>11, 12</sup>
<i>Oncology</i>	Non-Hodgkin's lymphoma	0.3 – 2.9 <sup>1, 2, 3</sup>	Anal cancer or anal intraepithelial dysplasia	0.4 – 1.6 <sup>1, 4, 5, 6, 7</sup>
			Lung cancer	
			Seminoma	
			Head and neck cancer	
			Hodgkin's lymphoma	0.3 – 2.9 <sup>1, 2, 3</sup>
			Castleman's disease	

Addressing Late HIV Diagnosis through Screening and Testing

Speciality	AIDS-defining conditions	HIV prev., %	Other conditions where HIV testing should be offered	HIV prev., %
<i>Gynaecology</i>	Cervical cancer	0.4 – 1.6 <sup>1,4,5,6,7</sup>	Vaginal intraepithelial neoplasia	
			Cervical intraepithelial neoplasia Grade 2 or above	
<i>Haematology</i>			Any unexplained blood dyscrasia including: <ul style="list-style-type: none"> <li>• thrombocytopenia</li> <li>• neutropenia</li> <li>• lymphopenia</li> </ul>	3.2 <sup>1</sup>
<i>Ophthalmology</i>	Cytomegalovirus retinitis		Infective retinal diseases including herpesviruses and toxoplasma	
			Any unexplained retinopathy	
<i>Ear, Nose and Throat</i>			ENT Lymphadenopathy of unknown cause	
			Chronic parotitis	
			Lymphoepithelial parotid cysts	
<i>Other</i>			Mononucleosis-like syndrome (primary HIV infection)	3.9 – 7.0 <sup>1,13,14,15</sup>
			Pyrexia of unknown origin	
			Any lymphadenopathy of unknown cause	
			Any sexually transmitted infection	4.1 <sup>1</sup>

Prev.; prevalence, ENT; Ear, nose and throat. <sup>1</sup>[70], <sup>2</sup>[71], <sup>3</sup>[72], <sup>4</sup>[73], <sup>5</sup>[74], <sup>6</sup>[75], <sup>7</sup>[76], <sup>8</sup>[77], <sup>9</sup>[78], <sup>10</sup>[79], <sup>11</sup>[80], <sup>12</sup>[81], <sup>13</sup>[82], <sup>14</sup>[83], <sup>15</sup>[84], <sup>16</sup>[85], <sup>17</sup>[86], <sup>18</sup>[87], <sup>19</sup>[88].

## Appendix 3

Summary of data from pilot studies expanding HIV testing in hospital acute medical admissions.

Study	Hospital (Geographical area)	Diagnosed HIV prevalence per 1000 individuals 15–59 years living in area	% tests offered (tests offered/ eligible population)	% uptake (tests performed/ tests offered)	% coverage (tests performed/ eligible population)	New HIV diagnoses per 1000 tests (number)	Cost per new diagnosis, £	Reference
HINTS	Homerton University Hospital (City and Hackney)	8.3	48.0 (628/1298)	70.1 (384/548)	29.6 (384/1298)	10.1 (4)	-	[13] <i>Evidence level IIb</i>
Routine HIV test offer	Leicester Royal Infirmary (Leicester City)	2.8	-	-	17.0 (938/5517)	10.7 (10)	-	[42] <i>Evidence level IIb</i>
Routine HIV test offer	Brighton and Sussex University Hospital (Brighton and Hove)	7.4	43.5 (1190/2735)	88.2 (1049/1190)	38.4 (1049/2735)	1.9 (2)	-	[41] <i>Evidence level IIa</i>
Anonymous			N/A	N/A	100.0 (3006/3006)	3.7 (11)	-	
Routine HIV test offer	Croydon General Hospital (Croydon)	4.8	-	84.0 (154/183)	32.5 (4122/12682)	4.1 (17)	1466*	[40] <i>Evidence level IIb</i>
RAPID project	UCLH (Camden and Islington)	7.4 (Cam.) 9.0 (Isl.)	25.3 (153/606)	88.2 (135/153)	22.3 (135/606)	22.2 (3)	1083	[89] <i>Evidence level IIb</i>
Routine HIV test offer	Royal Victoria Infirmary (Newcastle upon Tyne)	1.6	15.6 (586/3753)	82.8 (396/478)	10.6 (396/3753)	5.1 (2)	768*	[90] <i>Evidence level IIb</i>

\* no staff costs included; - data not reported.

## Appendix 4

Summary of data from pilot studies expanding HIV testing into primary care.

Geographical area	Intervention type	Number of practices	% tests offered (tests offered/eligible population)	% uptake (tests performed/tests offered)	New HIV diagnoses per 1000 tests (number)	Cost per new diagnosis, £	Reference
Hammersmith and Fulham	Routine HIV test offer to all patients	1	26.9 (1442/5352)	75.4 (1002/1329)	0.0 (0)	-	[13] <b>Evidence level IIb</b>
Haringey	Staff training in sexual health clinical skills	39	-	-	16.7 (39)	-	[53] <b>Evidence level IIa</b>
Hackney	RCT of staff training on offer of POCT for new registrants	40	24.9* (11180/44971)	44.5* (4978/11180)	2.2 (11)	-	[58] <b>Evidence level IIb</b>
Brighton and Hove	Routine HIV test offer to attendees of new patient health check	9	93.5 (2478/2651)	59.4 (1473/2478)	1.4 (2)	19403.70	[67] <b>Evidence level IIb</b>
Lewisham	Routine HIV test offer to new registrants	18	-	62.0 (2713/~4400)	7.0 (19)	1901.41	[67] <b>Evidence level IIb</b>
Wandsworth	Routine HIV offer to new registrants	-	-	48.0 (~3900/8146)	1.0 (4)	-	[54] <b>Evidence level IIb</b>
Blackpool	Routine HIV test offer to all patients	1	100.0 (475/475)	21.1 (100/475)	0.0 (0)	-	[91] <b>Evidence level IIb</b>
Manchester	Routine HIV test offer to new registrants	1	-	66.3 (303/475)	13.2 (4)	-	[91] <b>Evidence level IIb</b>
SE London	Routine serology HIV test offer to new registrants	5	78.5 (4925/6275)	18.4 (905/4925)	12.2 (11)	-	[91] <b>Evidence level IIb</b>
SE London	Routine POCT HIV test offer to new registrants	13	39.4 (6405/16241)	50.4 (3229/6405)	3.7 (12)	-	[91] <b>Evidence level IIb</b>

POCT, point of care test; RCT, randomised controlled trial.

\*POCT in intervention arm.



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