Barriers to testing for Human Immunodeficiency Virus infection in the United Kingdom

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Declaration of Originality

I hereby declare that the thesis submitted is my own work. All direct or indirect sources used are acknowledged as references. Where I have quoted from the work of others, the source is always given. I have acknowledged all main sources of help and where the thesis is based on work done by myself, jointly with others, I have made clear exactly what was done by others and what I have contributed myself. With the exception of such quotations, this thesis is entirely my own work.

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ABSTRACT

In recent years there has been an increased focus on biomedical interventions as a means of Human immunodeficiency Virus (HIV) prevention and the use of antiretroviral therapy (ART) has been a particularly successful tool in prevention efforts, with evidence for treatment in reducing HIV transmission. This is dependent on several factors including the early identification of those infected with HIV. In this thesis I will explore current challenges to testing for HIV in the UK by systematically reviewing current national levels of testing and investigating demographic characteristics associated with timing of diagnosis, testing practices and routes to diagnosis among those recently diagnosed with HIV in West London in order to identify barriers to increased and repeat testing for HIV in the UK. My findings show that guideline recommended testing levels are poor in most clinical settings and this is reflected in overall low HIV test coverage in the UK. HIV diagnosis at an earlier point in infection remains significantly associated with men who have sex with men (MSM) and White ethnicity and both patient and provider barriers act as ongoing challenges in earlier identification of HIV in all groups. Current testing practices are not enough to achieve equitable access to early diagnosis for HIV. Testing practices of clinicians, along with system challenges play an important role in HIV testing and changing these may be the most effective method of increasing earlier identification of HIV positive individuals in the UK.

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Glossary of abbreviations and acronyms

A

A&E – Accident and Emergency

AIDS - Acquired Immunodeficiency Syndrome

AMU – Acute Medical Unit

ANC - Antenatal Care

aOR - Adjusted Odds Ratio

C

CAPRISA - Centre for the AIDS programme of Research in South Africa

CAQDMS - Computer Assisted Qualitative Data Management Software

CHIVA - Children's HIV Association

CI - Confidence Interval

CNS - Clinical Nursing Specialist

D

DH - Department of Health

DNA – Did Not Attend

E

EACS - European AIDS Clinical Society

EBM - Evidence Based Medicine

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

ED - Emergency Department

ELISA - Enzyme-linked Immunosorbent Assay

F

FEM – Fixed Effect Model

G

GCP – Good Clinical Practice

GP – General Practice

GUM - Genitourinary Medicine

H

HA/ART - Highly Active/Anti-Retroviral Therapy

HINTS - HIV Testing in Non-Traditional Settings

HIV - Human Immunodeficiency Virus

HPA - Health Protection Agency (currently known as PHE)

HPTN - HIV Prevention Trials Network

I

ICHT - Imperial College NHS Healthcare Trust

IDU - Injecting Drug Users

iPrex - Pre-exposure Prophylaxis Initiative

IQR – Inter-quartile Range

IRAS – Integrated Research Application System

M

MSM - Men who have sex with men

N

NAAT - Nucleic Acid Amplification Testing

NHS - National Health Service

NICE - National Institute for Health and Care Excellence

NNRTI – Non-Nucleoside/tide reverse transcriptase inhibitor

O

OR - Odds Ratio

P

PEP - Post Exposure Prophylaxis

PEPSE - Post Exposure Prophylaxis following Sexual Exposure

PHE - Public Health England (formerly known as HPA)

PLWHA – People living with HIV/AIDS

PMTCT - Prevention of mother-to-child Transmission

POC/T - Point of Care/Test

PrEP - Pre-exposure Prophylaxis

R

REM- Random Effect Model

RCT - Randomised Control Trial

S

SH - Sexual Health

SOPHID - Survey of Prevalent HIV Infection Diagnosed

STI/D – Sexually Transmitted Infection/Disease

T

TAP - Treatment as Prevention

TB - Tuberculosis

THT - Terrance Higgins Trust

TOP - Termination of Pregnancy

U

UAI - Unprotected Anal intercourse

UK - United Kingdom

UK CAB - UK Community Advisory Board

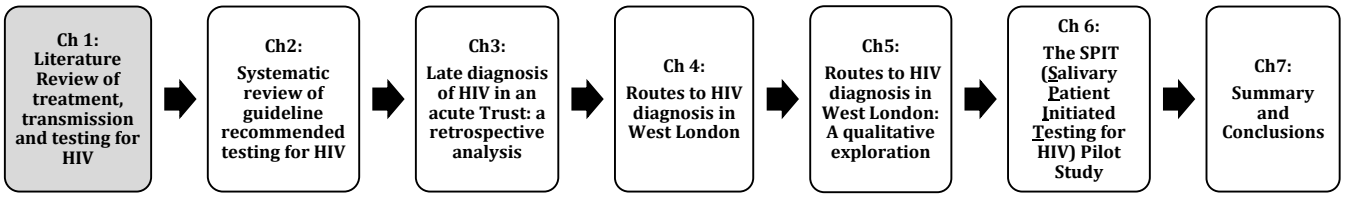
UTI – Urinary Tract Infection

UVA - Unprotected Vaginal/Anal intercourse

W

WHO – World Health Organisation

Chapter 1: Literature review of treatment, transmission and testing for HIV



INTRODUCTION

In the decades since the Human Immunodeficiency Virus (HIV) was first identified as the causative agent in the development of Acquired immune deficiency syndrome (AIDS) there has been a strong international response from the scientific community to mitigate the spread of this virus. Despite this however the HIV epidemic continues to pose a substantial problem for health in the United Kingdom (UK) and globally. Much of the research efforts over the past 30 years have focused on the prevention of transmission of the virus due to the challenges encountered in the development of an efficacious cure or vaccine for the infection.[1, 2] Although there has been much investigation, particularly early in the history of the pandemic, into non-biomedical strategies involving change in behaviours, the extent of the impact of such interventions has been difficult to measure and highly contested. Prevention strategies should be based on best available evidence and this has evolved over time, starting with basic preventive advice (including reduction in total number of sexual partners, consistent use of condoms during sexual intercourse and preventing needle sharing), testing and counselling and health protection measures such as ensuring a safe blood supply and avoidance of nosocomial transmission. In recent years however there has been increased focus on biomedical interventions, particularly treatment for people living with HIV/AIDS (PLWHA), and possibly the partners of PLWHA as a means of reducing HIV transmission. However, one of the key challenges in using treatment to prevent HIV transmission is the identification of PLWHA early in infection, which has been a challenge in the UK.

In this thesis I will start by reviewing the evidence for treatment as a means of reducing HIV transmission and then go onto address specific questions related to improving testing methods and models in the UK to

facilitate treatment-based prevention of HIV in subsequent chapters. I will review the evidence for the use of treatment as a means of reducing onwards HIV transmission, looking at the epidemiological evidence for the relationship between ART, reduced viral load, infectivity and the importance of this in the sexual transmission of HIV. I will then go on to review and investigate the effectiveness of current HIV testing practices, identify potential obstacles and explore an alternative model for optimising HIV testing in the UK.

HIV Treatment and HIV Transmission

The relationship of viral load and infectivity of HIV means that effective treatment with antiretrovirals reduces viral load and that as viral load is reduced in an individual the infectiousness of that individual is also reduced with this in turn reducing the risk of transmission of the virus through various transmission routes including sexual intercourse, intravenous or percutaneous transmission and vertical (mother-to-child) transmission.

Antiretrovirals, viral load and transmission

Before the introduction of ART as a form of treatment for HIV, an association was identified in maternal viral load and the risk of transmitting the virus onto the infant during pregnancy and in the perinatal period.[3, 4] A prospective cohort study of 701 HIV-1 positive pregnant women, conducted by the European Collaborative study across 19 centres in Europe, which aimed to describe factors associated with vertical transmission of the virus found that high levels of the p24 antigen (p24 antigenaemia) were significantly associated with an increase in the risk of mother-to-child HIV transmission. [5] Administration of ART to has become increasingly available to pregnant women world-wide and World Health Organisation (WHO) guidelines recommend the administration of Antiretroviral therapy (ART) to all pregnant women, regardless of viral load and to their babies in the first few months of life to reduce the risk of perinatal transmission of HIV.[6] On the basis of these early findings, the relationship between viral load and HIV transmission has been investigated more broadly and applied in interventions controlling transmission not just from mother to child, but through other routes of transmission.

Post exposure prophylaxis (PEP)

Post Exposure Prophylaxis (PEP) is a means of preventing HIV infection following suspected exposure to the virus. This involves the administration of a short course of ART to a recently exposed individual once

the virus has entered the body but before higher rates of viral replication are reached. Pathogenesis studies indicate that there may be a window of opportunity to abort HIV infection by inhibiting viral replication following an exposure. Once HIV crosses a mucosal barrier it may take 48–72 hours before HIV can be detected within regional lymph nodes and up to five days before HIV can be detected in blood. Animal models have shown that treatment will act to eliminate the small amounts of the virus at an early stage by inhibiting viral replication and therefore preventing latent HIV infection.[7, 8]

This method of preventing HIV infection through the use of antiretrovirals is used in post nosocomial or occupational percutaneous exposure, sexual exposure and in the prevention of mother-to-child transmission of HIV where neonates receive antiretrovirals following perinatal exposure to their HIV positive mothers. In 1997, the United States Centre of Disease Control and Prevention (CDC) Needle stick Surveillance group published the results of a case-control study of 698 healthcare workers who experienced occupational percutaneous HIV exposure, 33 of the participants were cases and the remaining 665 controls. After adjusting for other exposure factors associated with HIV infection, it was found that the adjusted odds ratio (aOR) for contracting HIV in case patients given prophylactic Zidovudine monotherapy was 0.19 (95% CI: 0.06-0.52) compared to controls. [9] Although a retrospective case-control trial is not an optimal design for assessing the efficacy of Zidovudine therapy in preventing HIV infection post exposure, a prospective placebo-controlled study has never been undertaken for ethical reasons and PEP following occupational percutaneous exposure is now routine practice in healthcare settings in North America [10] and European and UK guidelines also recommend HIV post-exposure prophylaxis as an essential method in the prevention of occupational HIV infection.[11]

Post-exposure prophylaxis following sexual exposure (PEPSE) is the administration of ART, usually a month long course of triple therapy, following a sexual exposure with a partner known to be HIV positive. This method is used in the UK as a means of reducing the risk of HIV transmission in an exposed individual. In a 2009 systematic review to determine the efficacy of PEPSE, no prospective RCT were identified.[12] The review concluded that it was not possible to determine the effectiveness due to lack of evidence. An observational PEPSE study undertaken in Brazil demonstrated that fewer HIV seroconversions occurred among individuals taking PEPSE compared with those who did not.[13] however this study was not powered to detect a difference in HIV incidence. Due to the lack of strong evidence in support of PEPSE, the latest review and guidelines for use of PEPSE in the UK recommend that a risk

benefit analysis is undertaken for each individual presenting following a sexual exposure to HIV. This should be based on the risk of transmission following the exposure, the risk of the partner being HIV-positive and the viral load of the source, if known.[14]

Although occupational PEP and PEPSE have become established methods in preventing HIV transmission in the scenarios described above, this method of treatment is unlikely to have the same impact on transmission in the far more common instances of sexual exposure to HIV where individuals are unaware of the HIV infection and this remains the primary driver of population level HIV transmission.

Pre-exposure prophylaxis (PrEP)

Pre-exposure prophylaxis (PrEP) is another form of HIV treatment as a means of preventing. In PrEP, individuals who are uninfected are given low dose ART before a potential exposure. This method of treatment in high-risk individuals has proven efficacious in reducing the transmission of HIV in randomised placebo-control trials such as those carried out by the Pre-exposure Prophylaxis Initiative (iPrEx). One such study measured the effect of PrEP in 2,499 HIV seronegative men and transgender women who have sex with men across 11 countries.[15] The study participants were randomly assigned to the PrEP arm, which involved the administration of a single daily tablet of Truvada (a combination of Tenofovir Disoproxil Fumarate and Emtricitabine), or the placebo arm, which involved the administration of a single daily tablet of the placebo. The participants were followed up for a median of 1.2 years from 2007 to 2009. During the follow up period 100 participants became infected with HIV; 36 in the treatment arm and 64 in the placebo arm, indicating a 44% reduction in the incidence of HIV (95% CI: 15%-63%), p=0.005. Investigators additionally analysed levels of adherence to the single daily dose regimen and found that despite self-reported adherence being high (around 90%), an analysis of a subsample of the drug group showed that drug levels were detectable in 51% of those that remained HIV seronegative and only in 9% of those who seroconverted. This increased the efficacy of the drug in individuals with detectable drug levels to 92% (95% CI: 40%-99%) p<0.001.

In addition to this, trials of topical PrEP based interventions in women have been undertaken to assess the efficacy of antiretroviral based vaginal microbicides such as the randomised placebo-controlled trial undertaken by the Centre for the AIDS programme of Research in South Africa (CAPRISA 004). This has

however only proven to infer modest amounts of protection from HIV infection, with Tenofovir gel reducing HIV acquisition by an estimated 39% overall. [16]

Concerns regarding ethics and cost of such programmes and unanswered questions around viral resistance remain an issue in the use of PrEP. Although there was no record of Tenofovir resistance in those using the Tenofovir gel and later seroconverting in the CAPRISA 004 trial, resistance was identified in the iPrEx trial. Two men with undetected, seronegative acute HIV infection who were recruited and randomised to the treatment arm later developed resistance to Emtracitibine.[17] Increasing HIV resistance in the roll out of PrEP based interventions is an important risk to consider particularly as drug adherence is rarely as high as that seen in the clinical trial setting. Currently, only around 37% of those in need of ART across the world receive treatment, the majority of these are in low and middle-income countries and therefore the ethics of administering ART to those who are uninfected as a means of prevention when a large proportion of those requiring treatment for life-saving purposes are not in receipt of it has been called into question.[18] These difficulties and unresolved questions makes the use of PrEP as a tool in HIV prevention contentious and means this form of treatment is especially difficult to roll out at a population level.

ART and genital HIV RNA concentration

In the post HAART era, an association was seen in the effective treatment of HIV positive individuals and reductions in their plasma viral load and importantly, in terms of sexual transmission of the virus, the level of viral shedding in genital secretions. Several prospective observational cohort and cross-sectional studies at this time illustrated this, showing correlations in blood plasma and genital tract concentrations of HIV-1 RNA with significant reductions in both vaginal and seminal HIV-1 shedding in those undergoing treatment.[19-26]

Antiretroviral treatment does not however result in total elimination of genital HIV-1 RNA shedding even in those with low or undetectable plasma viral levels. A cross-sectional study of thirty three men in Canada found a poor drug penetration of the non-nucleoside reverse transcriptase inhibitor (NNRTI), Efavirenz to seminal plasma in two (6.1%) of the men despite undetectable blood plasma concentrations of viral RNA[24] and a larger prospective study of 290 women conducted in California found 44 (15%) had

detectable cervical HIV-1 RNA levels despite plasma RNA level of <50 copies/ml, [23] highlighting the potential for viral transmission despite effective treatment and supressed blood viral concentrations.

Viral load and sexual transmission of HIV

Many studies directly identify associations in lower viral load and reduced risk of sexual transmission of HIV-1.[27-31] Despite definitions in high and low viral load varying between studies (>100,000 RNA copies/ml and <100,000 RNA copies/ml, 21,139 and 5,484 RNA copies/ml, 4.3 and 3.6 $\log_{10}$ RNA copies/ml) all illustrate significant differences in transmission seen in those with higher mean viral load compared to those with lower mean viral load and later studies, quantifying risk of sexual transmission of HIV at differing viral loads such as the mathematical model by Lignappa *et al.*[27] begin to characterise the relationship between HIV-1 RNA levels and HIV-1 infectiousness. This model was based on data collected from a large prospective cohort study, the Partners in Prevention HSV/HIV Transmission Study. The model assumes a linear relationship between log risk of HIV-1 transmission and $\log_{10}$ plasma HIV-1 RNA level with the solid line as the model-predicted risk of transmission and the dashed lines as 95% confidence intervals. The model predicts a reduction in transmission of between 37% and 50% when HIV-1 RNA levels are reduced by 0.5 $\log_{10}$ and 0.74 $\log_{10}$ respectively. These predicted levels were similar to those seen in other studies such as the HIV-1 serodiscordant couples study in the Rakai district of Uganda[32] and a Zambian study of HIV-1 serodiscordant couples. All of which illustrate that after controlling for other factors associated with HIV transmission, viral load is the strongest predictor of the risk of transmission.

Infectiousness in HIV is greatly variable due to the natural history of the disease, virological characteristics and the impact of antiretrovirals. In primary HIV infection viral load is on average at one of its highest points in the course of the infection. However, this period is relatively short (approximately 3-6 months) [29] in relation to the subsequent latent stage of infection which makes up the majority of an infected individual's life. In the latent stage viral load is much lower compared to the primary stage of infection. In the final stage of HIV infection when AIDS diseases occur, viral load again peaks to its highest point in infection and CD4 cell count/mm^3 is at its lowest. In terms of heterosexual transmission of HIV, patients at this stage of infection are at their most infectious however. [33]

In a retrospective cohort study of 235 monogamous serodiscordant couples conducted in the Rakai, Uganda, rates of sexual transmission of HIV per coital act were estimated according to the HIV positive partner's stage of infection.[30] It was found that transmission from those who had seroconverted in the past 2.5 months, in those 6-25 months before their death and in those between these periods to be 0.0015/coital act (95% CI: 0.0039-0.015), 0.0028/coital act (95% CI: 0.0015-0.0041) and 0.0007/coital act (95% CI: 0.0005-0.01), respectively. Indicating that late stage of infection, followed by early stage of infection, is the period of greatest transmission risk in this population. It is therefore important to take stage of infection into account when assessing the probability and the duration of stage into account in probability of viral transmission.

For HIV serodiscordant partnerships therefore, the index case's plasma viral load and the stage of HIV disease, particularly early and late stage, are the main virological factors contributing to increased risk of onward transmission. It is unclear however to what extent stage, duration and variations in viral load interact and contribute to overall transmission rates.

The first randomised control trial, measuring the efficacy of the use of ART in reducing heterosexual transmission of HIV in serodiscordant couples was terminated early in 2011 when the continuation of the trial was considered ethically inappropriate. The HIV Prevention Trials Network (HPTN) conducted a multicentre international trial, HPTN 052, to compare early versus delayed combination ART for patients with HIV-1 infection who had CD4 cell counts 350-550 cells/mm^3 and who were in stable sexual relationships with partners who were not infected.[34] 1,763 couples from 9 countries were recruited and randomised to receive early ART, immediately at the start of the trial or late ART , after a decline in CD4 cell count to <350 cell/mm^3, as per the WHO recommendations at the time.[35] A total of twenty-eight transmissions were virologically linked to the HIV-positive partner in the study. 1 transmission occurred in the early-therapy group (incidence rate, 0.1 per 100 person-years; 95% CI, 0.0-0.4) and 27 transmissions in the delayed-therapy group (incidence rate, 1.7 per 100 person-years; 95% CI, 1.1-2.5) This illustrated a relative reduction of virologically linked HIV transmission by 96% in those initiating immediate ART at higher CD4 cell counts than those initiating at lower CD4 cell counts. The populations described here, although from a number of countries were all heterosexual, outcomes in other groups such as men who have sex with men (MSM) or injecting drug users (IDU) have been explored. There is also a high rate of adherence seen in this study which is unlikely to be seen outside a clinical trial setting.

Adherence in ART is particularly important in the effective suppression of viral load and poor adherence can lead to substantially higher rates of transmission than those seen here and introduces an increased risk of the complication of resistance. Additionally the effect of risk compensation if this method of HIV prevention was rolled out at a population level would also have to be monitored. Rates of unprotected sexual intercourse, although controlled for, were not quantified for each of the arms in this trial so we cannot tell what impact this has had on the results. Although, the results from this study support the use of ART as part of a national strategy to help reduce the transmission of HIV-1, further controlled trials testing the impact of this on a population level are required to explore these unanswered questions.

Population level reduction in HIV transmission

Although empirical studies and mathematical models have proven the use of ART to be efficacious in the reduction of HIV transmission in stable serodiscordant couples, they do not inform us of the potential of ART to reduce the transmission of HIV at a population level and there are important caveats to the results of these clinical trials translating to foreseeable population level reduction in HIV transmission.

There has been evidence in recent years from observational studies to support the idea of treatment as a means of preventing the transmission of HIV. Several cross-sectional studies have reported reductions in population level transmission of HIV in the period following wide-spread use on antiretrovirals. A study undertaken in Taiwan assessed the transmission probability ratio in the Taiwanese population, before and after the implementation of a free-HAART policy.[36] Authors used a model of HIV surveillance results, which had been predicted by a modified back-calculation projection to fit the routine epidemiological data gathered in the period before, during and after implementation of free-HAART policy. Routine surveillance data on the incidence of Syphilis was used as a proxy to indicate levels of unprotected sex in the population. Model simulation results found that after free access to HAART was established, the estimated HIV transmission rate decreased by 53% (95% CI: 31%-65%) with incidence in the general population from 0.391 to 0.184 new cases per year. Although authors attempted to control for the various factors which could have confounded results in this analysis through use of rigours statistical methods and a flexible model, several factors remain unadjusted for and go to reduce the value of the findings of this study. The major confounding factor, of this study, was reductions in risky behaviour for which there was no accurate estimation for. The use of syphilis incidence surveillance data as a surrogate marker is an unreliable method for the quantification of rates of unprotected sex. Although Taiwan has a strong

surveillance system for detection of rates of HIV this is not the case for other sexually transmitted infections including syphilis. In many countries messages of safer sexual practice and behavioural change have played a large part in the reduction of HIV transmission[37-39] and this study has failed to adequately control for the impact of such patterns in behaviour change on HIV transmission rates in the Taiwanese population. Despite this, the collective findings of such similar studies and the biological evidence presented from earlier work indicate that ART may be playing a large role in the reduction of population level transmission of HIV.

Large cluster randomised controlled studies trialling the effect of the administration of ART to reduce HIV transmission are currently underway. One of these will be conducted by the HIV Prevention Trials Network, HPTN 071; PopART (Cluster randomised trial of the impact of a combination prevention package including early antiretroviral treatment on population-level HIV incidence in Zambia and South Africa) [40] will assess the impact of ART on population level HIV transmission. The study consists of 24 clusters in Zambia and South Africa and will run over a five year period. Of the twenty-four clusters, 8 will be randomly allocated to receive a combination prevention programme of HIV Voluntary counselling and testing (VCT), male circumcision to all HIV-negative men tested for HIV, counselling on risk reduction, condom provision and the offer of immediate ART to all those testing HIV-positive. A further 8 clusters will be offered the same combination intervention package but with the provision of ART according to current WHO guidelines (CD4 cell count <350 cell/mm^3). The final 8 clusters will act as the control arm of the study with HIV counselling, testing and treatment provided at the national standard of care. The trial hopes to assess the impact of immediate treatment of patients compared to current international guidelines and national guidelines in Zambia and South Africa. Clinical outcomes, cost-effectiveness and reduction in transmission analyses will be undertaken to assess the population effect of treatment as a means of preventing HIV. Until the results of this and other such population intervention studies are released however, an accurate assessment of the population impact of treatment as a means of prevention for HIV will remain difficult.

Improved clinical outcomes in early treatment

The benefits of HIV treatment are not limited to reductions in transmission. Since ART has become available to millions of HIV-infected individuals around the world, the life expectancy for those living with HIV has increased dramatically with rates of HIV associated disease also decreasing. By limiting the

extent of HIV replication in the body, ART allows an increase in CD4 cell count, strengthening the immune response and increasing the body's ability to defend against the opportunistic infections associated with infection. Despite this, variations in individuals' immune responses to antiretroviral therapy, the point at which treatment should be commenced to confer the best possible clinical outcomes for the HIV-positive patient, HIV resistance to ART and poor adherence to medication continues to be a challenge in optimising patient outcomes and public health in HIV.[41]

There is an strong body of evidence to indicate that the initiation of ART earlier rather than later in HIV infection results in improved outcomes for the patient.[42-45] Since the introduction of ART, the only randomised clinical trial to assess treatment outcomes in patients initiating therapy at different CD4 cell count thresholds was terminated early. The trial compared those who initiated ART at CD4 cell counts 201-350 cells/mm^3 with those patients in who treatment was deferred until then <200 cells/mm^3 (as recommended by World Health Organisation guidelines at the time). When interim analysis showed that deferral of therapy resulted in a 4-fold increase in mortality ($p=0.001$) and a 2-fold increase in risk of tuberculosis ($p<0.01$) the trial was terminated.

As established above, there is a substantial body of evidence for the potential of ART as a means of preventing HIV transmission however, treatment remains a comparatively costly and resource consuming intervention which has still to be proved efficacious at a population level. Although treatment may not be in itself a magic bullet for HIV elimination in many settings, it has proven an essential component of not only the clinical management of HIV-positive patients but also the control of HIV transmission and when used as part of the 'tool-box' of HIV prevention interventions it may prove to be the key to feature in future HIV control initiatives.

Sexual behaviour and HIV transmission

The global HIV epidemic is fuelled by heterosexual transmission, which accounts for over 80% of the 36 million people now infected with HIV.[46] HIV-1 has a low transmissibility compared to other sexually transmitted infections but despite the global effort to reduce rates of viral transmission, incidence remains high and factors relating to the sexual transmission of the virus continue to pose major challenges in the reduction of HIV transmission.

Antiretrovirals and sexual behaviour

Aside from important aspects contributing to population level transmission and to a lesser extent, biological risk factors that can impact on transmission in individual serodiscordant relationships, more distal contributor to sexual behaviours, such as risk perception have also been identified as having a potential impact on HIV transmission. Risk perception in HIV relates to how individuals regard their risk of acquiring HIV, transmitting HIV and the consequences of infection. Gerald J S Wilde posited a theory of risk homeostasis in 1998 which goes some way to explain this. This theory proposes that people adapt their behaviour to changes in their environmental conditions, therefore when they perceive a higher risk they are more cautious and, conversely, when they perceive a reduction in risk they are less so. Although originally developed to explain changes in risk behaviour associated with road safety in high income countries such as Canada and Sweden, Eaton LA *et al* have adapted the theoretical model for HIV in their review of the literature on risk compensation to biomedical interventions for HIV (Figure 1). This theory underlies much of the research for risk compensation in HIV.[47]

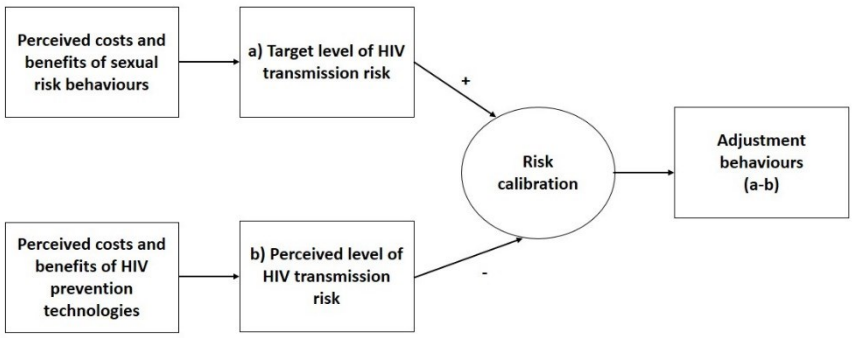


Figure 1: Adapted model of risk compensation and sexual risk behaviours from Wilde's risk homeostasis model by Eaton LA et al.[47]

There is also evidence from several ecological studies indicating resurgence in high-risk sexual behaviour following the routine administration ART to HIV-positive people.[48-50] This pattern is particularly seen in MSM populations in high income countries.[51, 52] A cross-sectional study of the effects of ART on HIV incidence amongst MSM in San Francisco was the first to assess the impact of the availability of ART on

HIV incidence at a population level.[53] The study used survey results from 26,176 different MSM in San Francisco to assess trends in sexual behaviour from 1994 to 1999 tracking two markers of sexual risk behaviour: reporting of condom use during anal sex and reporting of number of sexual partners. Trends in incidence of rectal gonorrhoea were taken from routine surveillance data and used as a surrogate marker of rates of unprotected sex alongside self-reporting in interviews. The number of MSM who were using ART increased from 278 (4%) in 1995 to 3,959 (54%) in 1999. Interviews showed that the percentage of MSM who reported always using condoms in the preceding 6 month when engaging in anal intercourse decreased from 70% in 1994 to 54% in 1999 ($p<0.001$). Over the same period the number of men reporting both unprotected anal sex and multiple sexual partners increased from 24% to 45% ($p<0.001$). Due to the design and chosen outcomes and measures in this study there are significant weaknesses and potential biases and although the results illustrate a trend of increasing HIV incidence from the period of 1997 to 1999 and a pattern of increased high risk behaviour, the association of this with ART uptake was not measured but merely observed as a parallel increase, so whether or not the use of ART is a factor in change in sexual risk behaviour remains unclear.

HIV status awareness and sexual behaviour

Differences in sexual behaviour in those who are aware of their HIV-positive status compared to those who are not may also contribute to HIV transmission. This is of value in increasing uptake of HIV testing as regular testing with post-test counselling is the only way for individuals to become aware of their HIV status and for the associated benefits of this to be inferred.

If an individual is aware of their HIV status and is promptly and correctly referred into HIV care services they are likely to commence ART at a clinically appropriate time. As discussed earlier, this reduces their risk of morbidity and mortality and knowledge of status is therefore of benefit to an individual from a clinical perspective. The public health implications of status awareness are also important as those who are aware of their HIV positive status are less likely to transmit HIV than those who are not. The reasons for this include therapy with antiretrovirals and change in sexual behaviour and decreased transmission rate.

A 2002 US cohort study of 66 MSM who had recently seroconverted (in the 6 month period since their last HIV test) aimed to identify whether changes in sexual behaviour after diagnosis of HIV was observed by

estimating sexual risk behaviour in those aware and unaware of their HIV status. Sexual risk behaviour questionnaires were administered in recent seroconverters before receiving the results of their HIV test, at one month and quarterly thereafter for a period of eighteen months. The results showed receipt of a HIV positive diagnosis was associated with a significant reduction in high risk sexual behaviour in the follow up period from the baseline.[54] Subsequent studies in the USA and in Africa have also shown similar findings.[55, 56] Only one study identified did not show this trend. This was a cross-sectional survey of 397 patients in an HIV in clinic Seattle, [57] which found high risk sexual behaviour in those patients who knew themselves to be HIV-positive and were in medical care with reported rates of unprotected anal and vaginal intercourse at 27%, 20% and 24% for MSM, heterosexual men and women, respectively.

A review conducted on 11 studies, 6 of which compared the sexual behaviours of HIV-positive aware groups to HIV-positive unaware groups (between-group comparisons) and the remaining 5 compared the sexual behaviours of the same cohort of HIV-positive participants before and after becoming aware of their status (within-group comparison).[58] The primary outcome assessed was difference in sexual risk behaviour between groups, defined as self-reported unprotected vaginal or anal (UVA) intercourse in the specified time period. The results of this analysis showed a 53% reduction in UVA intercourse (95% CI: 45-60%). When this was adjusted for results from primary studies, where reporting of UVA intercourse was with another HIV-positive person, the rate was found to be a 68% (95% CI: 59%-76%) reduction in UVA in those aware of their HIV status compared to those unaware (Table 1). The findings of this review and meta-analysis are based on primary studies with outcomes which were self-reported, leaving scope for respondent bias. Additionally, authors were unable to examine the *number* of sex partners placed at risk by HIV-positive aware and unaware persons, which is the primary outcome of interest in assessing risk of population transmission. Additionally, other risk factors including viral load, stage of infection, and concomitant STD, which also contribute a difference in transmission risk, could not be assessed.

	Model Based on Unadjusted Data From Primary Studies	**Model Based on Adjusted Data From Primary Studies**
All findings pooled (*k*=11)	53% (45%-60%)	68% (59%-76%)
Between-group comparison (*k*=6)	60% (58%-63%)	72% (59%-80%)
Within-subjects comparison (*k*=5)	37% (27%-46%)	64% (57%-71%)
Male Participants (*k*=7)	53% (40%-63%)	70% (58%-79%)
Female participants (*k*=4)	55% (48%-62%)	66% (44%-80%)

Table 1: Effect Sizes of the random-effects models: Reduction in prevalence (%) of UAV in HIV-positive Aware relative to HIV-positive Unaware Persons and 95% confidence intervals. Findings taken from Marks G et al. [58]

A similar picture emerges from studies examining STD acquisition rates as a proxy marker of unprotected sexual contact between HIV-positive aware and unaware persons.[59-61] A retrospective cohort study conducted by Otten *et al* compared rates of sexually transmitted disease diagnosis in 331 HIV-positive patients and 666 HIV-negative patients prior to testing, diagnosis and counselling and at 11 to 60 days following post-test counselling in Miami, Florida. Results showed a 29% reduction in rates of diagnosed STI during the follow-up period in those testing HIV-positive however the study was not appropriately powered to detect this change with 95% CI (-67%-10%).[62] These findings highlight the value of HIV testing and counselling as an essential HIV prevention tool and the importance of undiagnosed HIV infection as a risk factor in HIV transmission.

HIV TESTING IN THE UK

Detection of HIV infection depends on several important factors including the appropriate test, frequency of testing, ease of access of testing facilities, effective counselling method and patient and provider attitudes to testing. These factors vary highly between countries and in different settings. In the next part of the chapter I will look at the impact of these factors on HIV and discuss the impact of this on HIV diagnosis, transmission and clinical management in the UK.

HIV tests

HIV tests fall into three categories; antibody tests which detect the presence of the immunoglobulins made by the body in response to infection, antigen tests which detect the presence of the HIV (p24) or HIV RNA and so called 'fourth generation' tests which are a combination of both types of test and have the ability to detect the presence of viral antigen and humoral antibodies simultaneously. The tests vary in sensitivity and specificity, time taken to receive results and cost.

The p24 antigen is usually detectable before antibodies to the virus are. Antibody tests can on average be used to confirm the presence of HIV infection and rule out the possibility of infection in 97% of cases after a 'window period' of 3 months. The window period is a period where the level of antibody in the blood of an infected individual is not necessarily detectable. The window period varies between tests and is 1–6 months for tests detecting HIV antibody, however most people seroconvert (develop antibodies to the HIV virus) within 30 days of infection. Antigen tests characteristically detect the presence of HIV infection earlier, at around 1-4 weeks of infection and therefore have a much shorter window period than antibody tests. Due to their comparatively low specificity however, p24 antigen test are rarely used in isolation to detect HIV infection but are mainly used as a component of fourth generation HIV test. False negative test results increase the risk of undiagnosed HIV infection in the population whilst false positive results cause an increase in unnecessary additional testing and patient distress therefore tests used to diagnose for HIV infection require a high degree of both sensitivity and specificity.

There are two types of antibody test used in routine practice for testing for HIV in the UK. One involves taking a blood sample by venepuncture and screening by assay, usually ELISA (enzyme-linked immunosorbent assay) but occasionally Western blot and has a 1-3 day waiting period for results, with this test being able to detect anti-HIV IgM as well as IgG antibodies.The second type of antibody test is the

rapid test, also known as a rapid point of care (POC) test where a blood sample is taken by finger prick. POC tests carry the benefits of producing a result within minutes, can be used on a wide variety of tissues including saliva, making them easier to use in non-clinical settings, areas where high-throughput screening is required and in situations where venepuncture is refused as a method of testing. POC tests have a lower sensitivity and specificity than conventional antibody tests however and therefore confirmation of test results through laboratory assays is recommended in guidelines. All HIV test results returned and diagnosed as positive whether they are diagnosed using POCT or ELISA are confirmed with a second test using Western Blot to detect the presence of antibodies to HIV.[63]

Direct detection of HIV RNA using a method known as Nucleic Acid Amplification Testing (NAAT) is another method of testing for HIV but is rarely used as a clinical tool for the diagnosis of HIV due to its relatively high cost and limited benefits over antibody or antigen testing. It is used as a tool to monitor viral load for the clinical assessment and management of HIV-positive patients[64] and as a method of HIV testing in the screening of donations from blood donors and occasionally as a means of identifying HIV infection in the neonates of HIV-positive mothers who will carry maternal antibodies to HIV for a period of up to 18 months after birth and who may also be receiving PEP which can result in inaccurate results of antibody and antigen tests.[65]

HIV and testing in the United Kingdom

Provider initiated testing and counselling, is a form of 'opt-out' HIV testing where health providers test in a routine manner rather than the patient requesting a test. This method is thought to be a more effective way of increasing testing as patients who are at risk of acquiring HIV rarely request HIV tests.[70] The WHO guidance for provider-initiated HIV testing and counselling in low-level HIV epidemics recommends that healthcare providers should not initiate HIV testing and counselling to all persons attending all health facilities in setting with low-levels of HIV prevalence, such as the UK, but rather concentrate on those adults, adolescents and children with:

"…*signs or symptoms suggestive of underlying HIV infection."*[70]

Provider-initiated testing was also recommended in some health facilities attended by high prevalence or high risk groups even in low population prevalence settings such as in STI services, services for most at risk populations (including sex workers, their clients, men who have sex with men, injecting drug users,

prisoners or migrants) and antenatal care services where the national aim is for the elimination of mother-to-child-transmission of HIV.[66] WHO guidance also recommends the provision of simplified pre-test information for provider-initiated HIV testing and counselling in health facilities. In this model, individuals attending a given healthcare setting are offered and recommended an HIV test as standard but can decline.

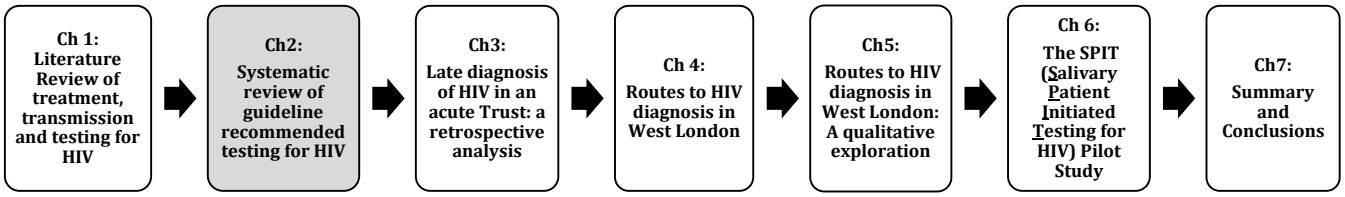
In the United Kingdom a targeted testing approach, in accordance with WHO guidelines is in place. Routine provider-initiated testing has been recommended to all antenatal care attendees since 1999 and all sexual health clinic attendees and in Termination of Pregnancy (TOP) services since 2001. By 2010, these made up the majority of all HIV tests administered in the UK.[67] By the end of 2011, the number of people infected with HIV in the UK reached an estimated 91,500 (credible interval of 85,400 – 99,000) and despite changes in UK guidelines recommending universal HIV testing not only for all women attending antenatal care and all sexual health clinic attendees but additionally all general medical admissions and those registering with a general practitioner in areas of greater than 2 per 1,000 population prevalence among 15-59 year olds.[64] Twenty-four percent (Credible interval 19%-30%) of those living with HIV in the UK remain undiagnosed and are therefore unaware of their infection and of those who are diagnosed with HIV 47% (2,990/6,360) are diagnosed with a CD4 cell count of <350 cells/mm^3.[68]

JUSTIFICATION OF RESEARCH

The findings from this literature review show that those aware of their HIV status are less likely to engage in high risk sexual behaviour, particularly with individuals known to be HIV negative. An individual's knowledge of their HIV serostatus can therefore in itself be an effective preventative intervention and this is supported by a strong body of evidence. Additionally, those identified as being HIV-positive and who are referred into care, are able to receive ART earlier than those who are not, which reduces their infectivity. In order to achieve effective HIV prevention interventions we therefore require comprehensive counselling and testing services, which routinely test those who are at high risk of infection and ensure appropriate referral into care for those individuals who are diagnosed with HIV. The substantial level of undiagnosed HIV and late presentation of the infection in the UK is an indication of the challenges that remain in these areas. Establishing a culture of high levels of frequent HIV testing requires sustained intervention at multiple levels.

The evidence I have encountered in this review is in support of earlier HIV diagnosis as an essential component in improving patient outcomes and reducing HIV transmission. In this thesis I will therefore start by exploring current testing coverage in the UK and investigate the challenges to HIV testing which still exist and may be contributing to low levels of HIV diagnosis in the UK.

Chapter 2: Systematic Review of levels of Guideline Recommended Testing for HIV



As established in the previous chapter, timely identification of those who are HIV-positive and appropriate referral into care services is essential for the reduction of both HIV associated morbidity and mortality, and the prevention of onwards transmission of the virus. A high level (47%) of late diagnosis of HIV, defined as presentation with an AIDS diagnosis or CD4 count <350 cells/mm^3 continues to illustrate the problem created by inadequate HIV testing in the UK.[68] Although challenges remain in ensuring universal screening of those attending facilities such as SH\GUM and ANC clinics, some of which have been described earlier in Chapter 1, HIV testing in these settings has come to make up the vast majority of testing which occurs in the UK accounting for 47% and 31% of total HIV tests in the UK respectively.[68] This leads us to look to other clinical setting in order to accurately assess where testing for HIV is ineffective in identifying those individuals who are HIV positive in a timely manner.

INTRODUCTION

UK National Guidelines for HIV Testing 2008

The national guidelines for HIV testing (briefly described in Chapter 1) were published in October 2008. The guidelines were published by BHIVA and written in collaboration with the British Infection Society (BIS) and the British Association for Sexual Health and HIV (BASHH). The guidelines were intended to facilitate an increase in HIV testing in all healthcare settings and reduce the proportion of individuals with undiagnosed HIV infection. The authors state the reason for the need of their publication as being a) misconceptions regarding HIV testing remaining a hindrance to increased testing; b) the importance of both the individual patient and public health benefits of increased testing and c) the need for up-to-date

guidance that would enable any clinician to perform an HIV test within good clinical practice, thereby encouraging the 'normalisation' of HIV testing.

The guidelines themselves were written further to extensive evidence gathering, review and consultation amongst key interest groups and organisations including those representing government (Department of Health Expert Advisory Group on AIDS), patient and community advocates (CHIVA, UK CAB) and clinical groups (Royal Colleges of General Practitioners, Nursing, Physicians and Paediatrics and Child Health) and include a lay representative.[64] After the compilation of the guidelines a web consultation process was undertaken whereby comments on the guidance was made by interested persons and groups and responses made by collaborators, this consultation was also used as a tool to review the guidance prior to publication.

In July 2012 NICE Accreditation Advisory Committee accredited BHIVA for the process of development of national HIV testing guidance. Indicating that NICE recognises that:

- The processes used to produce the BHIVA UK national guidelines are rigorous, transparent and systematic;
- Individuals from all relevant stakeholder groups, including patients, were involved in developing guidance;
- The methods of balancing benefits and risks in developing the recommendations are well described;
- The process for updating, maintaining and improving the quality of the guidance and process of external peer review are well described.

In March 2011, NICE additionally published Public Health Guidance 33 and 34, with recommendations for 'Increasing the uptake of HIV testing to reduce undiagnosed infection and prevent transmission among Black Africans/men who have sex with men'. The recommendations reiterate those made in the BHIVA publication and build on these with implementation tools to provide practical means of facilitating increased HIV testing.[69, 70]

Subsequent to their compilation, the UK National Guidelines for HIV testing were published in *HIV Medicine*, announced in a press release in September 2008 and have been available through the BHIVA website since that time. There was additionally a letter circulated to by the Chief Medical Officer (CMO), to all Trusts and family doctors following the release of these guidelines.

Key recommendations being available in an openly accessible form to all through a 5-page format for download. The BHIVA publication *HIV Medicine,* although a widely available peer-reviewed journal is "–specifically aimed at researchers and clinicians with the responsibility for treating HIV seropositive patients." making it a poor tool for the dissemination of guidelines to wider specialities where there is the greatest risk of low HIV testing levels. An audit of clinician awareness of the latest HIV testing guidelines conducted in one hospital, found that 67% of physicians working in non-HIV specialities were unaware of the publication of these guidelines[71] providing some indication of the low impact that the guidelines made in the wider clinical settings that they were aimed for. The audit was however undertaken in an area of low HIV prevalence, with a poor response rate (21.1%) and at only two months following the publication of the guidelines. It is quite possible that over time, content of the guidelines would have been more widely circulated and implemented by clinicians.

Levels of HIV testing in the UK

Given the extensive collaboration used to generate the national guidelines and their endorsement by a range of organisations including NICE, there has been an apparently limited adoption of them outside of GUM/SH and ANC settings. The relatively small proportion of testing undertaken in these settings has led many to redub these settings as 'Non-routine settings' or 'Non-specialist settings' and in 2011, led to the development of a large, pan-London study: HIV Testing in Non-traditional settings Study (HINTS). The study aimed to assess the levels of HIV testing in these settings across a number of hospitals and primary health care clinics in London where patients were routinely offered the option of an HIV test in A&E, Acute medical admission, out-patient departments and primary care facilities and found that 66.8% (61.8-75.4%) of patients in these settings accepted HIV testing when offered.[72] This provides an illustration of the levels of HIV testing that can be achieved in routine clinical settings but relied on HIV testing being offered consecutively to all patients in line with national guidelines for HIV testing which does not appear to be the reality of HIV testing practice in the majority of non-routine HIV testing settings

in the UK.[68] There was no additional assessment of the extent of HIV test offer by health providers and therefore the study did not provide a realistic depiction of current HIV testing in non-routine settings.

As previously described only 22% of total HIV tests administered in the UK occur in non-routine settings however, currently there is no routine method of monitoring levels of HIV testing in these settings (i.e. the number of those eligible for HIV testing who receive a test) as that available for routine settings through sentinel clinic data collated by PHE. This poses a challenge in increasing the amount of testing in these settings as we are currently unaware of where, how and why guideline recommendations are not being met and cannot ascertain how this may be contributing to low levels of HIV testing or the identification of HIV positive individuals at an earlier point in their infection.

Systematic review as a method of assessing the level of HIV testing in non-specialist settings

A systematic review is defined by the Cochrane Collaboration Glossary as:

"A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review." [73]

The origin of the systematic review lies in the evidence-based medicine (EBM) movement, the key principles of which are formulating questions on the best course of clinical practice and searching for, critically appraising and making a decision based on the assessment of this evidence.[74] And in keeping with EBM, systematic reviews have been increasingly used as a means of informing best practice in the UK through organisation such as The Cochrane Collaboration, which was established in 1993. The purpose of the systematic review is:

- To resolve conflicting evidence;
- Address questions where clinical practice is uncertain;
- Highlight a need for future research.

This description also states that use of systematic reviews is "– to explore variations in practice." And "-confirm the appropriateness of current practice."[9] Systematic reviews are useful in these instances due to the wide scope of their application, rigorous and explicit methodology and broad variation in their means

of analysis, helping to answer a range of questions relating to clinical practice. However, the widely encompassing methodology of systematic reviews also makes them susceptible to poor execution particularly if applied to the wrong type of question.

Although originally designed and tailored to assess evidence of specific study designs associated with interventions (e.g. RCT and Cohort Studies), systematic reviews have increasingly been used to assess non-interventional methodologies, including observational studies.[74]

In this systematic review I have aimed to use the available evidence generated from an explicit search and selection of the literature to assess the levels of routine HIV testing in guideline recommended, non-routine settings in the UK and analyse and summarise the extent of the implementation of national guidelines in these settings.

METHODS

Components of the systematic review: Review title, question and objectives

For the execution of an effective systematic review there is a need for the formulation of a thorough protocol, which will ensure a reduction of the impact of authors' biases, promotion of transparency of methods and processes, reduction in the potential for duplication and allow peer review of the planned methods.[75]

Ideally, when formulating a protocol there should be no changes made subsequent to the protocol being agreed upon by all parties involved in the search strategy and in order to ensure that there is limited need to make changes to the protocol, it is important to run a preliminary search with a limited search criteria solely to establish the existence of the literature relevant to the question or assess if the question is truly suited to being answered through this methodology.

These preliminary searches carry a risk of introducing bias early on in the systematic review process by exposing researchers to initial results and may result in a change in the protocol, biasing the findings towards the generation of articles presenting positive results. For this reason it is highly important that the preliminary search, if undertaken, is used solely to establish that undertaking the systematic review to answer the question is viable. The means of assessing how much bias is introduced into the systematic review process by conducting a search before establishing a clear protocol is not accurately described

however as this is down to the individual researcher it can be largely subjective. For this reason, many endorse the method of no searches before the formulation of a clear protocol and making no changes to this protocol thereafter.[75]

Despite this, it was felt appropriate that before the development of a protocol for this systematic review a preliminary search should be undertaken to assess the level of evidence available for the question and whether it is a feasible systematic review question to undertake. The components of a protocol include a background, objectives and most importantly, methods. The method of a protocol details the eligibility criteria of studies including types of studies, participants, interventions and outcome measures. The method additionally includes a detailed description of the search strategy and data collection.[76]

The protocol devised on the basis of a preliminary search can be found in Appendix A. This includes a title, question, review objectives and summary of inclusion and exclusion criteria. This is the tool employed in the selection process when deciding which studies should be incorporated in the systematic review and sets out the key components that studies are assessed on in answering the review question of levels of HIV testing in non-routine settings. Despite the systematic review question being specific it could potentially be answered by collection of the evidence from a broad range of studies and this is reflected in the broad eligibility criteria and search strategy employed. Due to the need to accurately assess the level of guideline recommended HIV testing being undertaken in non-specialist settings across the UK, a range of studies with varying design can be identified. This broad approach allows for a more comprehensive summary of the evidence and assessment of the findings across the different types of settings and populations. However, it does create difficulty during the analysis process due to the inevitable heterogeneity of the articles identified and extracted, which will be discussed in more detail later in this chapter but is still in keeping with the standard for the systematic review of observational studies.[77]

Components of the systematic review: Search for studies

The initial step in the execution of a search for the systematic review is the identification of a source or sources for the location of studies. The source used should be able to maximise the chance of identifying all relevant studies for answering the research question and in doing so, reduce the risk of bias and ensure the findings from the review are generalizable. Additionally, the identification and description of a

clear source or sources for the location of the studies used in the review is an essential step in helping to ensure that the results of the review are reproducible at the study identification stage.

In identifying the sources to be used for the location of studies for a systematic review, one should choose the sources which have maximum sensitivity (that is the ability of the source to correctly identify studies which are useful in answering the study question) and specificity (the ability of the source to correctly not produce any studies that are not useful in answering the study question) in locating studies. Considering the reviewer selection method of the systematic review (i.e. the reviewer being responsible for the screening of all studies identified regardless of their source) a source broad enough to maximise sensitivity at the expense of specificity is a valid tool to use in identifying the location of studies to be used in the review.

With these considerations in mind and the need for a convenient and centralised source from which to access the articles for the review – particularly considering the importance of ensuring the search can be replicated simultaneously, by a second reviewer, OvidSP was the chosen tool to identify the articles for this review.

OvidSP is an online bibliographic database which also acts as a specialist search tool, making it easy to record and execute searches in several online literature database sources. Amongst the largest of these sources is Medline (Medical Literature Analysis and Retrieval System Online), which is produced by the United States National Library of Medicine and has an index of more than 21.6 million publication records from approximately 5,400 life science and biomedical science journals since 1946. In addition to Medline, OvidSP provides access to the following databases: Embase -Biomedical and pharmacological international peer reviewed journals; Health Management Information Consortium (HMIC) – Health and social care management articles from DH library and information service and Kings Fund library service (UK focus); PsychINFO – Psychology, social, behavioural and health science journals with an emphasis on original research, amongst others. The above listed sources were selected to search through OvidSP as Ovid MEDLINE® In-Process & Other Non-Indexed Citations and Ovid MEDLINE® (1946 to present), Embase (1974 to present date), HMIC Health Management Information Consortium (1979 to present date) and PsycINFO (2002 to present date) and the combined search terms seen in Table 1 were run with the option for automatic removal of duplicate results, where the same reference is presented in more

than one of the databases selected for the search. To enhance validity of findings, this search was run by another reviewer, independently, with total results generated recorded and compared at each stage of the search process.

In addition to the OvidSP search of the published literature, BHIVA conference abstracts 2009-2012 and HIV testing published in an annual HIV Medicine supplement and reports published by PHE and DH on testing for HIV were also hand searched, independently by two reviewers. This was undertaken alongside the search of the published literature as, due to the recent publication of the BHIVA guidelines, many of the studies collecting data on HIV testing after this period are likely to be on-going or recently completed with the likelihood that many might not be yet peer reviewed and published. These choices chosen for hand search are UK specific reports reporting data on HIV testing and conferences where unpublished HIV testing data of relevant our review question is likely to be published.

Guideline recommended HIV test coverage in the UK

What is the level of adherence to guideline recommended testing for HIV in the UK?

1. (HIV or Human immunodeficiency virus).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, an, ui, tc, id, tm]
2. test$3.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, an, ui, tc, id, tm]
3. (UK or United Kingdom or England or Northern Ireland or Scotland or Wales).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, an, ui, tc, id, tm]
4. 1 and 2 and 3
5. remove duplicates from 4

Table 1: Ovid search used to identify relevant articles with search term combinations

Components of the systematic review: Screening of studies

Following the elimination of duplicates, the next stage of the search process is the title and abstract screen. To maximise sensitivity for this step of the screening process, abstracts were only rejected where it is certain that the criteria being assessed will result in the rejection of the study from inclusion in final studies and so this was based on the exclusion criteria of the review protocol. This process is illustrated in Figure 1, in a flowchart for criteria of exclusion.

The remaining abstracts retained for complete article review were screened for inclusion. There was also a title screen of bibliographic references of each of these articles to identify additional sources of data for inclusion that might have not been included. No bibliographic references identified independently from this process were eligible for final inclusion in the review indicating that the initial search was accurate in generating references for inclusion and that few articles eligible for inclusion were missed.

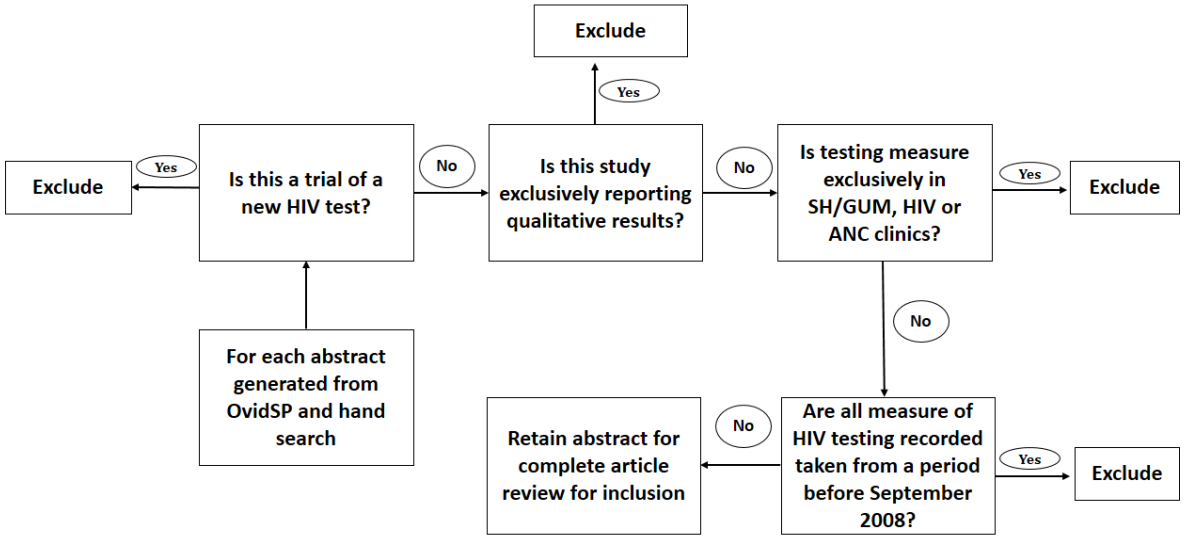


Figure 1: Flowchart of process of exclusion for title and abstract screen of references generated from OvidSP and hand search

First and second reviewer compared findings from the screening of the 155 articles and these are displayed in Table 2. Disparate results were reviewed by both reviewers and final decision for inclusion was made by first reviewer. The level of first and second reviewer agreement at screening is displayed in Table 2. There was a degree of discrepancy in both the inclusion and exclusion of articles between both reviewers with reviewer 1 and 2 independently including 23% and 34% and excluding 77% and 66% of articles screened respectively. This level of disparity may indicate that the protocol or inclusion and exclusion criteria for the screening process were unclear or not robust enough due to a high level of heterogeneity in studies.

Formal statistical methods for the measure of inter-reviewer agreement include Cohen's kappa coefficient. This is considered to be a more robust assessment of inter-reviewer agreement than simple percentages as it accounts for the degree of inter-reviewer discrepancy that may be due to chance. The Cohen's kappa statistic for the inter-reviewer agreement here is 0.5881, indicating that there is 58.81% agreement between reviewer 1 and 2. Due to variation in the application of inter-reviewer agreement assessments there is no established 'cut-off' point or level agreed upon as an acceptable level of agreement or discrepancy. However some authors recommend interpreting this value as 'fair agreement'[78] or 'moderate agreement'[79]overall.

Number of articles included by reviewer 1 independently (%)	Number of articles excluded by reviewer 1 independently (%)	Number of articles included by both independently (%)	Number of articles excluded by both independently (%)	Number of articles included by reviewer 2 independently (%)	Number of articles excluded by reviewer 2 independently (%)
36 (23)	119 (77)	15 (10)	88 (57)	52 (34)	103 (66)

Table 2: Inter-reviewer agreement on article inclusion and exclusion following full article screen (n=155). Abstract screen to Article screen

Where articles might otherwise be included for want of key missing data, first authors were contacted to retrieve this information with a blanket date for inclusion of data received as response for all authors contacted. Author contact was thought to be a legitimate and established means to ascertaining extra information relevant to a review.[80, 81]

Following the execution of the search criteria for the review and the screening process to exclude articles a summary of the pathway taken in identifying the papers for the review is created and presented. This summary of the number of articles generated in the search and included following the screening procedure described above is presented as recommended by PRISMA standards for systematic reviews[82] in Figure 2.

Components of the systematic review: Data extraction

All articles included for final data synthesis were reviewed and common variables were extracted. Key outcome variables extracted from the articles identified are the number of people who were tested for HIV, the number of people eligible to test for HIV, the number of people who were eligible for HIV testing who were offered an HIV test and finally the number of people tested for HIV who had a positive test result. Other data extracted included; type of article (i.e. abstract or complete article), risk group, primary testing outcome, exclusion criteria, time period, duration, population, setting (diagnosed HIV prevalence per 1, 000 population 15-59 year olds), number of centres, type of centre, method, measure/reporting

method. For increased validity, this process was undertaken by reviewer 1 and 2 independently, with any discrepancies discussed by both and final decision on inclusion being made by reviewer 1.

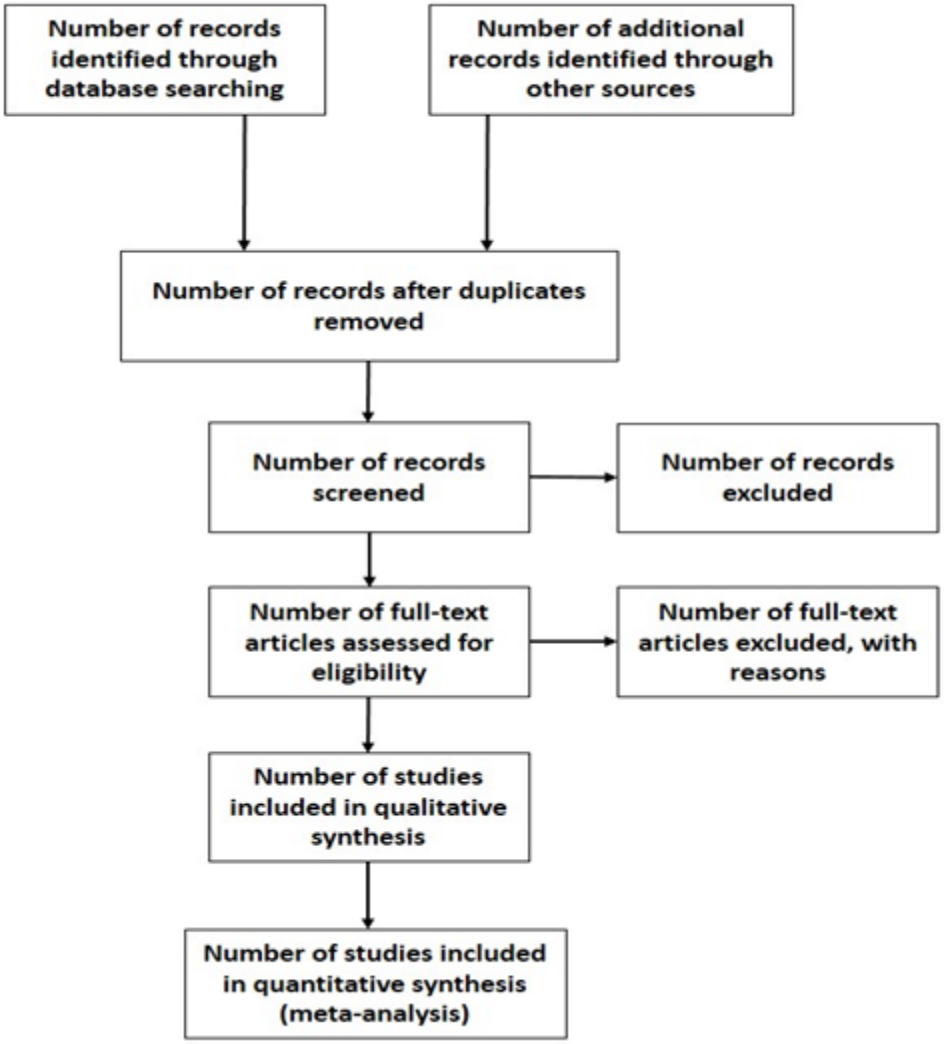


Figure 2: The flow diagram of different phases of a systematic review search. Taken from Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement [82]

Components of the systematic review: Data synthesis

The purpose of preliminary data synthesis is to organise the findings from included studies and describe patterns across the studies. This requires stratification of studies by characteristics important for outcomes, tabulation of the extracted data for ease of classification and comparison and a textual description of the findings.

Secondary and tertiary data synthesis requires the exploration of relationships between study characteristics and their findings, exploration of variations in these and identification and investigation of

any heterogeneity, in order to develop theories of plausible explanations for difference observed. This can be assessed to some extent through the use of quantitative techniques such as meta- analysis to summarise and estimate results across studies and meta-regression for the exploration of the contribution of variation in this summary.

Meta-analysis

Meta-analysis is a quantitative method of combining results of independent studies, exploring heterogeneity, and synthesizing a summary statistic for the combined studies where appropriate.[83]

In order to generate individual summary estimates for the primary outcome (a: proportion of those eligible for testing who are tested for HIV), data was extracted and proportion tested estimate (P_i) was calculated for each study as:

$$P_i = n_{i/} N_i$$

Where n_i represents the total number of people tested and N_i represents the total number of those eligible for testing. Clopper-Pearson (exact) confidence intervals (CI) were then calculated for this proportion in each study. Confidence intervals were capped at either 0, if they fell below 0 and 1 if they exceeded 1 for presentation alongside proportions.[84]

This method was also used to calculate proportion estimates and confidence intervals for secondary outcomes (b-d: proportion of those eligible for HIV testing offered an HIV test; proportion of those offered an HIV test who accept testing/are tested for HIV and; proportion of those tested for HIV who are found to be HIV positive) where this data was available. All proportion estimates were then converted to percentages before using this aggregate percentage for the meta-analysis.

A random effect model (REM) meta-analysis of the proportion estimates for test coverage was undertaken. REM meta-analysis was chosen due to the observational nature of the studies included in the review, with studies here likely to have a large amount of heterogeneity and therefore a model that allows for between-study variability in the calculation of overall effect estimate would be more a more appropriate fit than a fixed effect model (FEM), where only the in-study variance is taken into account.

Meta-regression

Meta-regression is used to assess the impact of covariates on effect estimate using regression techniques. This is a particularly useful tool when assessing meta-analysis results with high amounts of heterogeneity. Univariate meta-regression was therefore undertaken to investigate the variation seen in overall testing coverage estimate, controlling for patient group, study location, opt-in vs opt-out and service model and test type used. Proportions were transformed to log odds and standard errors for these log odds were generated for meta-analysis with results back transformed (exponentiated) for presentation as odds. Where covariates were found to contribute significantly (at the 5% significance level), the percentage of between-study variability explained by the covariate ($\mathbf{R^2}$) was calculated as:

$$R^2 = 1 - (\tau^2 \text{ with covariate} / \tau^2 \text{ without covariate})$$

Where τ^2 is the estimate of between study variance. The complete STATA command code generated and used for this analysis is available as Appendix B (Complete STATA code for final meta-analysis, written by Sarah Gerver and Gabriela Gomez and adapted by Rahma Elmahdi).

Both the meta-analysis and meta-regression for the final 30 studies were undertaken using STATA 12. The command **cii** was used to calculate proportion estimates and 95% Clopper-Pearson confidence intervals and the **metan** command was used for the REM meta-analysis for each study, stratified by group. Following conversion of proportion estimates to log odds and calculation of the standard error of the log odds, the **metareg** command was used to investigate the impact of individual covariates on the effect estimate.

RESULTS

Search results

A total of 1,226 references were screened and after exclusion of duplicates and a title and abstract screen, 163 full text articles were evaluated for full inclusion. Of these, 30 reports that measured levels of HIV testing in a range of recommended settings were identified (Figure 3). Fourteen were cross-sectional studies or retrospective studies (audits) from hospital settings using either case note review or extraction of data from electronic or paper records. Data from 12 were in journal publications and data from the remaining 18 studies were extracted from published reports or conference abstracts. Ten studies were in patients diagnosed with an indicator disease and 20 in people attending services where routine HIV

testing was suggested due to diagnosed prevalence in the local population. Key study characteristics are presented in Table 3: Characteristics of Studies Included: Methods, Measures and Testing Levels and all variables extracted for each study can be found in Appendix C: Complete data tables for final studies identified for inclusion, stratified by HIV testing patient group ('Person diagnosed with a disease indicative of possible HIV infection' and 'Persons attending services where routine HIV screening should be undertaken').

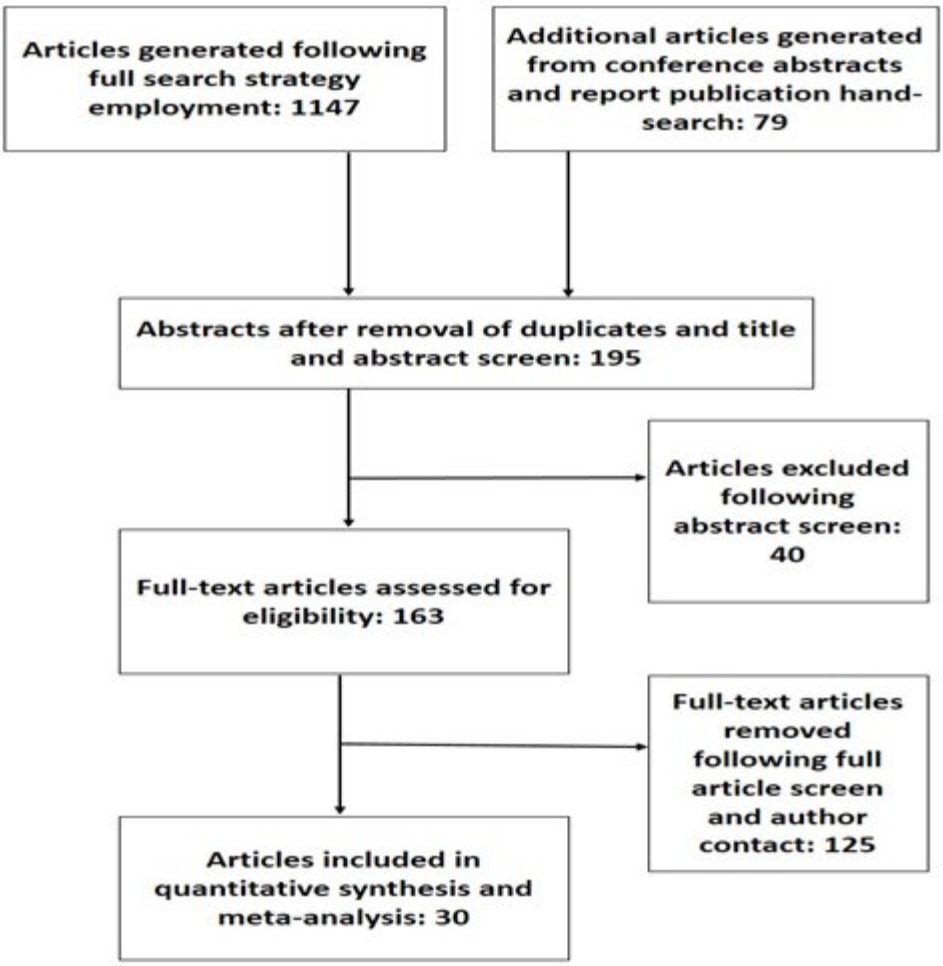


Figure 3: Flow diagram of search strategy and final article inclusion for data synthesis and meta-analysis

Author	Risk group	Setting (diagnosed HIV prevalence per 1,000 population 15-59 year olds) *	Methods	Number eligible to test	Number offered test	Number tested	Number testing positive
Persons diagnosed with a disease indicative of HIV infection							
Gupta, N.D. & Lechelt, M. (2011) [97]	Inpatients with indicator diseases (tuberculosis, hepatitis B, hepatitis C, cervical intraepithelial neoplasia (grade I/II), lymphoma, anal cancer, seminoma, aspergillosis or	South-west Essex (1.28)	Electronic record audit of attendees attending one secondary care hospital	557	33	33	Not reported

	Castleman's disease)						
Thomas William, S., *et al.* (2011) [98]	Patients with indicator disease (tuberculosis)	Birmingham and Solihull (Birmingham East & North; 1.5, Heart of Birmingham; 3.29, South Birmingham; 1.66; Solihull; 0.58)	Retrospective audit	194	Not reported	91	Not reported
Hsu, D., *et al.* (2012) [99]	Primary care patients presenting with glandular fever-like illness	South London (Lambeth 13.28, Southwark; 10.29)	Retrospective audit of patients attending 72 primary care clinics	1045	Not reported	118	3
Page, I., *et al.* (2011) [100]	Patients with indicator disease (tuberculosis,	Blackpool (3.41)	Retrospective audit of patients attending one secondary care hospital	156	Not reported	32	Not reported

	hepatitis B, hepatitis C, lymphoma)						
Thomson-Glover, R., *et al.* (2011) [101]	Patients with indicator disease (hepatitis B, hepatitis C, candida stomatitis)	Warrington (0.6)	Case-note audit of patients attending two secondary care hospitals	249	Not reported	15	0
Thorburn, F. (2012) [102]	Patients with indicator disease (diagnosed with tuberculosis)	Glasgow (1.7)	Retrospective case-note review of TB patients attending one tertiary care clinic	338	Not reported	221	9
Vas, A., *et al.* (2012) [103]	Patients with indicator disease (tuberculosis, hepatitis B, hepatitis C)	Manchester (5.22)	Retrospective case-note review of patients attending one secondary care hospital	91	13	9*	Not reported
Byrne, L., *et al.* (2011) [104]	Patients admitted to acute medical	London (Newham; 8.12,	Retrospective case-note review of patients attending	43	Not reported	17	2

	unit with community-acquired pneumonia	Tower Hamlets; 5.94)	one acute medical admissions unit				
Manavi, K., Gautam, N. (2012) [105]	Patients diagnosed with clinical indicator conditions as specified in UK HIV testing guidelines	Birmingham (3.29)	Retrospective case note review of patients attending one secondary care hospital	967	Not reported	97	1
Dodd, M. et al (2013) [106]	Patients with an HIV indicator illness in the presenting complaint or past medical history.	Sheffield (1.4)	Retrospective case note review of patients in one General Intensive Care Unit	307	Not reported	45	3
Persons attending recommended testing settings in high prevalence areas							
Burns, F., *et al.* (2012) [107]	Acute medical admissions	London (5.24)	Prospective, consecutive HIV test offer to patients	606	282	135	3

			attending one acute medical admissions unit				
Chan, S.Y., *et al.* (2011) [108]	Acute medical admissions	Croydon (4.45)	Prospective offer of HIV test to patients attending one acute medical admissions unit	101	101	84	0
Rayment, M., *et al.* (2012) [86]	Acute Care unit and Dermatology outpatient clinic	London (City and Hackney (8.25)	Prospective study of patients attending one acute care unit	1223	548	384	4
Perry, N., *et al.* (2011) [109]	Acute medical admissions	Brighton & Hove PCT (7.57)	Prospective HIV test offer to patients attending one acute medical admissions unit	3913	1553	1413	2
Bryce, G., (2009) [110]	Patients newly registering with GP	Brighton & Hove PCT (7.57)	Prospective HIV test offer to patients attending nine primary care clinics	2478	Not reported	1473	2
Ashby, J., *et al.* (2012) [111]	Polyclinic attendees in high prevalence area	West London (Kensington & Chelsea; 8.3, Hammersmith &	Prospective study of patients attending one polyclinic	302	93	71	0

		Fulham; 8.5, Westminster; 7.01)					
Ellis, S., *et al.* (2011) [112]	Acute medical admissions	Newcastle Upon Tyne (1.61)	Prospective audit of patients attending one acute medical admissions unit	3645	478	396	2
Rudran, B., *et al.* (2011) [113]	Acute medical admissions	Bournemouth and Poole (2.32)	Retrospective case-note review of patients attending one acute medical admissions unit	198	3	3	Not reported
Leber, W., *et al.* (2012) [114]	Patients newly registering with GP	Hackney (8.25)	Cluster randomised control trial of patients attending 40 primary care units	28274	6607	3213	7
Bassett, D., *et al.* (2012) [115]	Acute medical admissions	Manchester (5.22)	Prospective case-note review of patients attending one acute medical admissions	429	134	117	Not reported
Rosenvinge, M., *et al.* (2010) [116]	Women attending termination of pregnancy services	Wandsworth (4.91)	Retrospective review of HIV testing of patients who	870	844	702	1

			attended two termination of pregnancy clinic				
Garrard, N., *et al.* (2010) [117]	Women attending termination of pregnancy service	Southwark (10.39) and Lambeth (13.28)	Prospective, consecutive test offer to patients attending one termination of pregnancy clinic	2,831	Not reported	972	5
Barbour, A., *et al.* (2012) [118]	Patients admitted to acute medical admissions	Croydon (4.45)	Prospective intervention at one acute medical unit	3709	Not reported**	1390	7
Rycroft, J., *et al.* (2012) [119]	Acute medical admissions	Greenwich (5.58)	Retrospective audit of patients who attended one acute medical admissions	970	Not reported	43	3
Page, I., *et al.* (2011) [100]	Acute medical admissions	Blackpool (3.41)	Retrospective audit of patients who attended one secondary care hospital	13,999	Not reported	72	Not reported
French, S., *et al.* (2012) [120]	Patients newly registering with GP	Southwark (10.39), Lewisham (7.03), Lambeth (13.28)	Prospective study of patients attending 13 primary care clinics	16,241	6405	3229	12

French, S., *et al.* (2012) 5[120]	Patients newly registering with GP	Southwark (10.39), Lewisham (7.03), Lambeth (13.28)	Prospective study of patients attending 5 primary care clinics	6275	4925	905	11
Tillet, S., *et al.* (2012) [121]	Acute medical admissions	Tower Hamlets (5.94)	Prospective study of patients attending one secondary care hospital	1596	Not reported	241	2
Griffin, A., *et al.* (2011) [122]	Patient newly registering with GP	Manchester (5.22)	Prospective study of patients attending one primary care clinic	457	Not reported	303	2
Palfreeman, A., *et al.* (2013) [123]	Patients attending admitted to AMU	Leicester (3.22)	Prospective study of patients admitted to AMU	17226	Not reported	2542	29

Table 3: Characteristics of Studies Included: Methods, Measures and Testing Levels

HIV test coverage results

Figure 4 (a-g) shows the pooled estimates for the percentage of eligible patients who received an HIV test across all studies and studies stratified by Type of HIV Test (POCT or blood serology), Testing Strategy (opt-in or opt-out), Delivery model (standard, previous staff training or testing by HIV specialist), Location of study (London or not London), Study Type (retrospective or prospective) and Patient Group (people presenting with a disease indicative of HIV infection or people attending clinical setting where HIV testing should be routine.) for each study where this data was available. The meta-analysis showed the overall pooled effect estimate of HIV testing across all 30 studies (Figure 4a) was 27.18% (95% CI: 22. 36%-32%). This was highest in Chan *et al.* at 83.17% (95% CI: 74.42%-89.99%) lowest in Page *et al.* at 0.51% (0.4%-0.65%). There was a great deal of heterogeneity identified in these studies with an overall I^2 = 99.9%.

For meta-analysis by stratification by both Test Type and Testing Strategy there are fewer studies incorporated in the analysis due to no reporting of this data in the studies. These studies were excluded from the analysis and forest plots for ease of presentation. There were 13 studies reporting the type of testing undertaken (POCT or blood serology) and the result of the meta-analysis for test coverage when stratified by Test Type (Figure 4g) shows a higher test coverage with a pooled subtotal effect estimate of 34.95% (95% CI: 21.56%-48.34%) in studies testing using blood serology and only 31.8% (95% CI: 24.73%-38.87%) in those studies testing for HV using POCT. Twenty-one studies reporting Testing Strategy were incorporated in a meta-analysis and results of these (Figure 4b) show no difference in pooled estimates of test coverage level with 29.3% (95% CI: 22.44%-35.63%) in studies reporting opt-out testing and 31% (95% CI: 18.3%-43.7%) in those reporting opt-in testing.

For the remaining covariates, including Location, Delivery model, Study type and Patient group there was data available for all 30 studies and this was incorporated into stratified meta-analyses. When stratified by Location (Figure 4d), there appeared to be a higher pooled estimate for test coverage in London with 30.06% (95% CI: 23.68%-36.54%) which was lower in studies measuring test coverage outside of London at 24.63% (95% CI: 17.25%-32%). When stratified by Delivery Model (Figure 4c), the highest pooled estimates of test coverage are seen in those studies employing HIV specialists in patient testing at 42.77% (95% CI: 13.09%-72.45%), with test coverage in studies reporting standard testing methods at

26.45% (95% CI: 19.94%-32.96%) and lowest reported test coverage seen in studies using some form of staff education with 23.17% (95% CI: 18.29%-28.6%). There was also a higher pooled estimate of test coverage seen in studies reporting HIV testing in prospective studies at 31.62% (95% CI: 26.16%-36.37%) compared to test coverage in retrospective studies at 22.36% (95% CI: 13.07%-31.66%) when stratified by Study Type (Figure 4e). When stratified by Patient Group (Figure 4f), there was a lower pooled estimate for test coverage in people diagnosed with diseases indicative of HIV infection 22.39% (95% CI: 13.92%-30.86%) than patients attending clinical settings where HIV testing should be routine 29.47% (95% CI: 23.58%-35.37%). Figure 4 is divided into parts a-g below including:

Figure 4a: Forest plot of test coverage across all studies (n=30)

Figure 4b: Forest plot of test coverage by testing strategy

Figure 4c: Forest plot of test coverage by delivery model

Figure 4d: Forest plot of test coverage by test location

Figure 4e: Forest plot of test coverage by study type

Figure 4f: Forest plot of test coverage by patient group

Figure 4g: Forest plot of test coverage by test type

Figure 4a: Forest plot of test coverage across all studies (n=30)

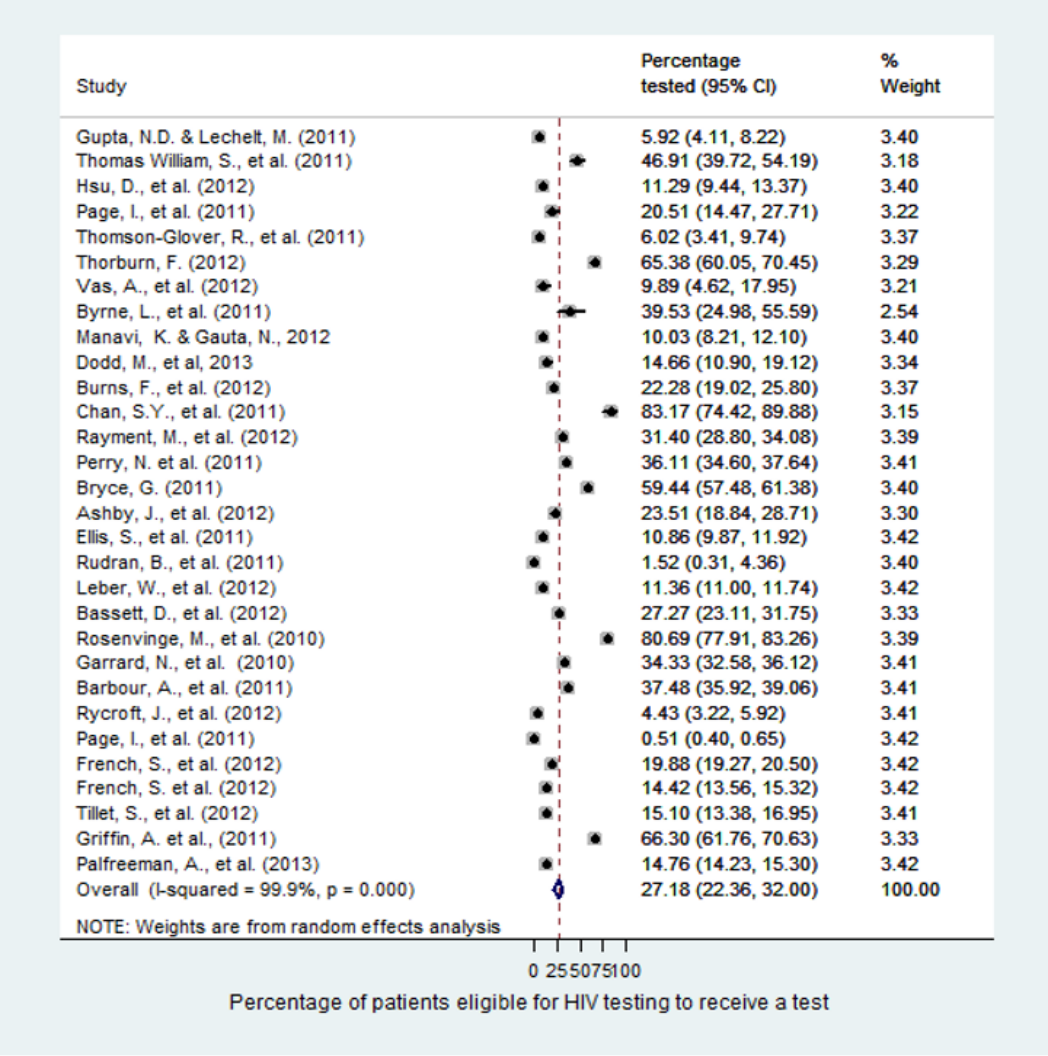


Figure 4b: Forest plot of test coverage by testing strategy

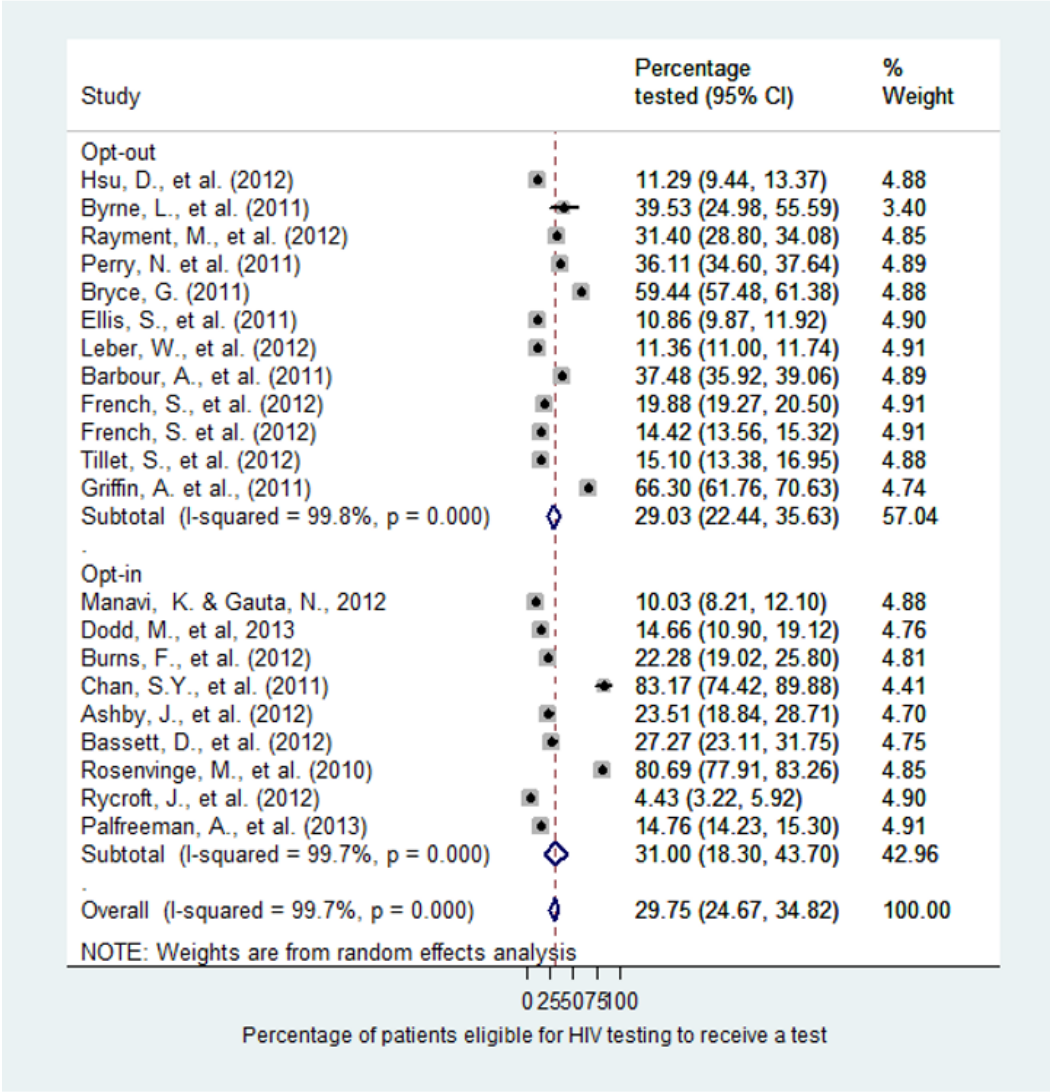


Figure 4c: Forest plot of test coverage by delivery model

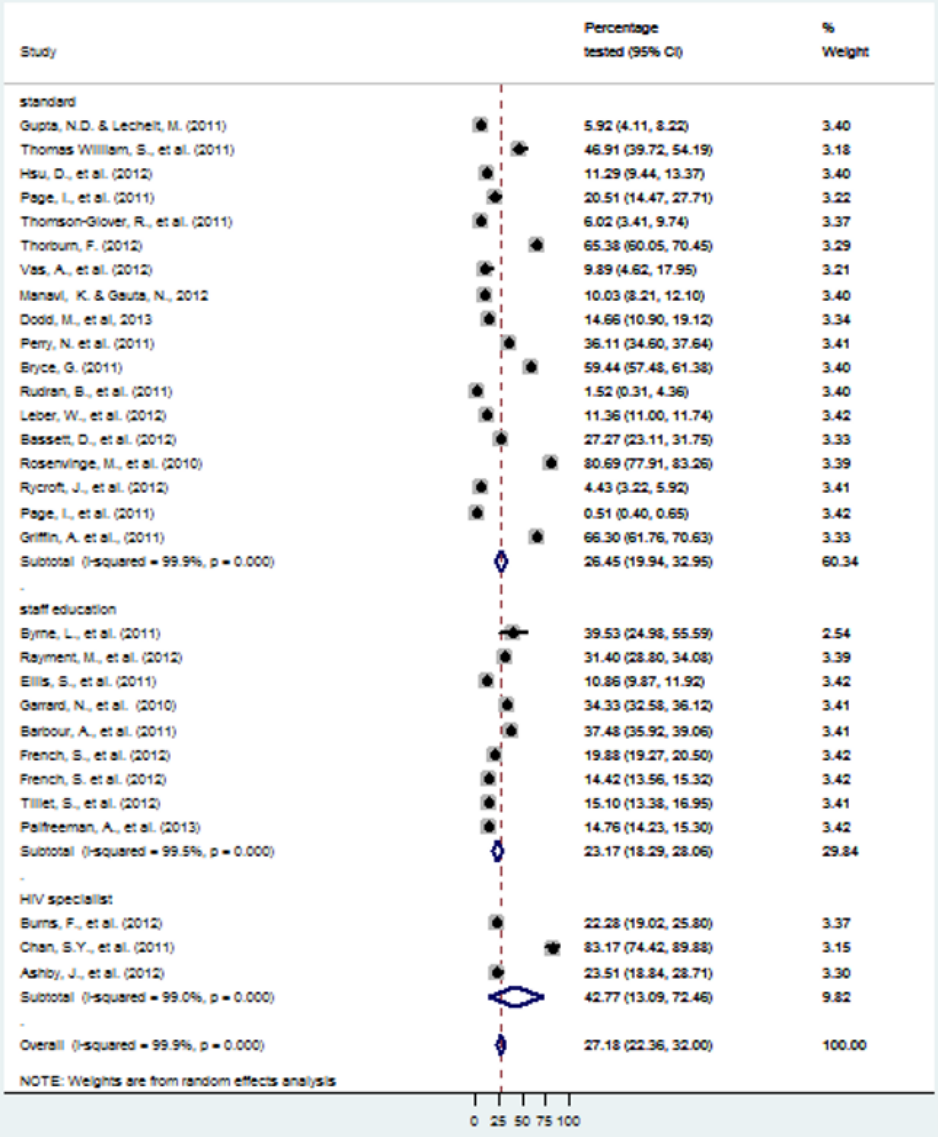


Figure 4d: Forest plot of test coverage by test location

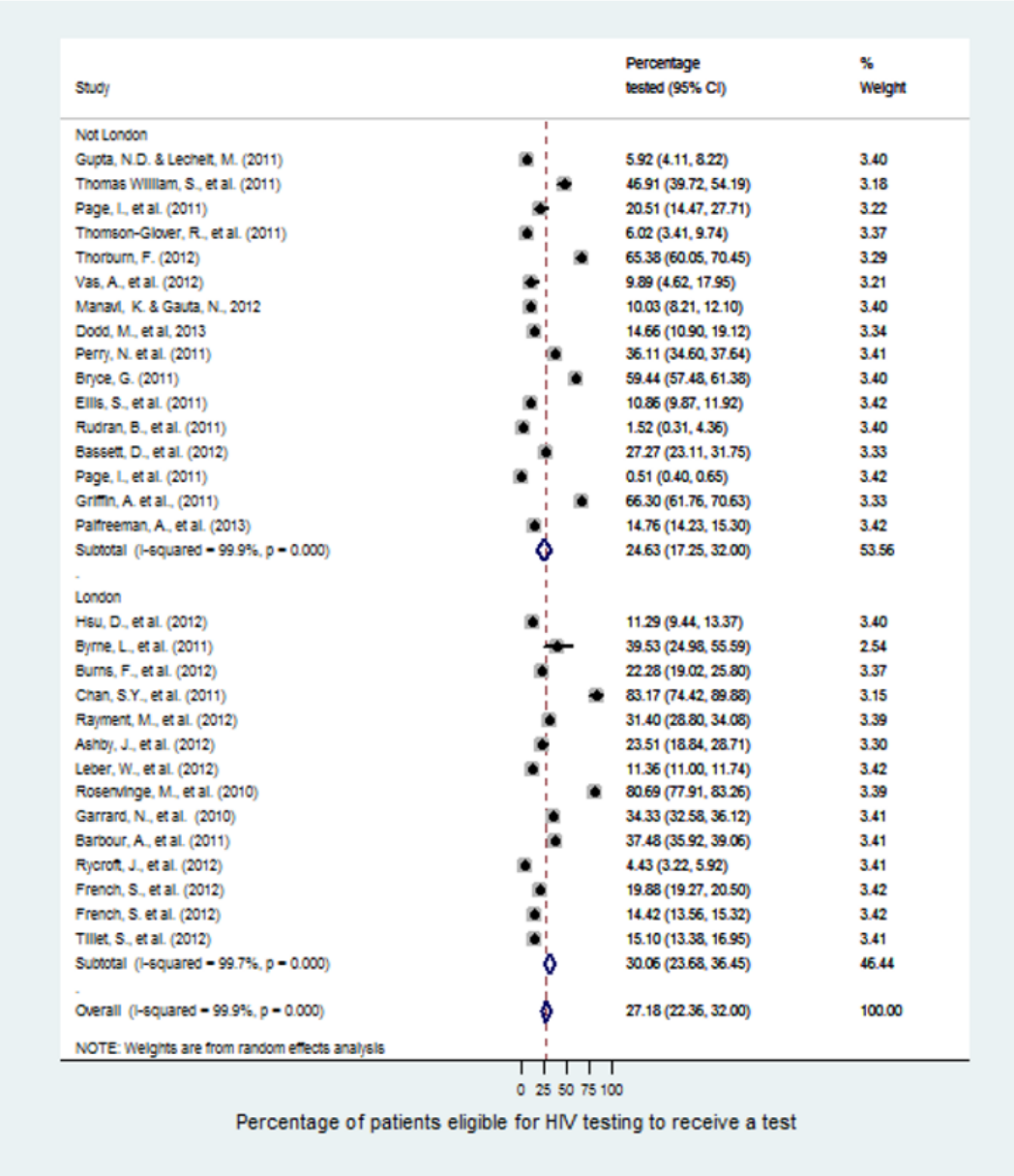


Figure 4e: Forest plot of test coverage by study type

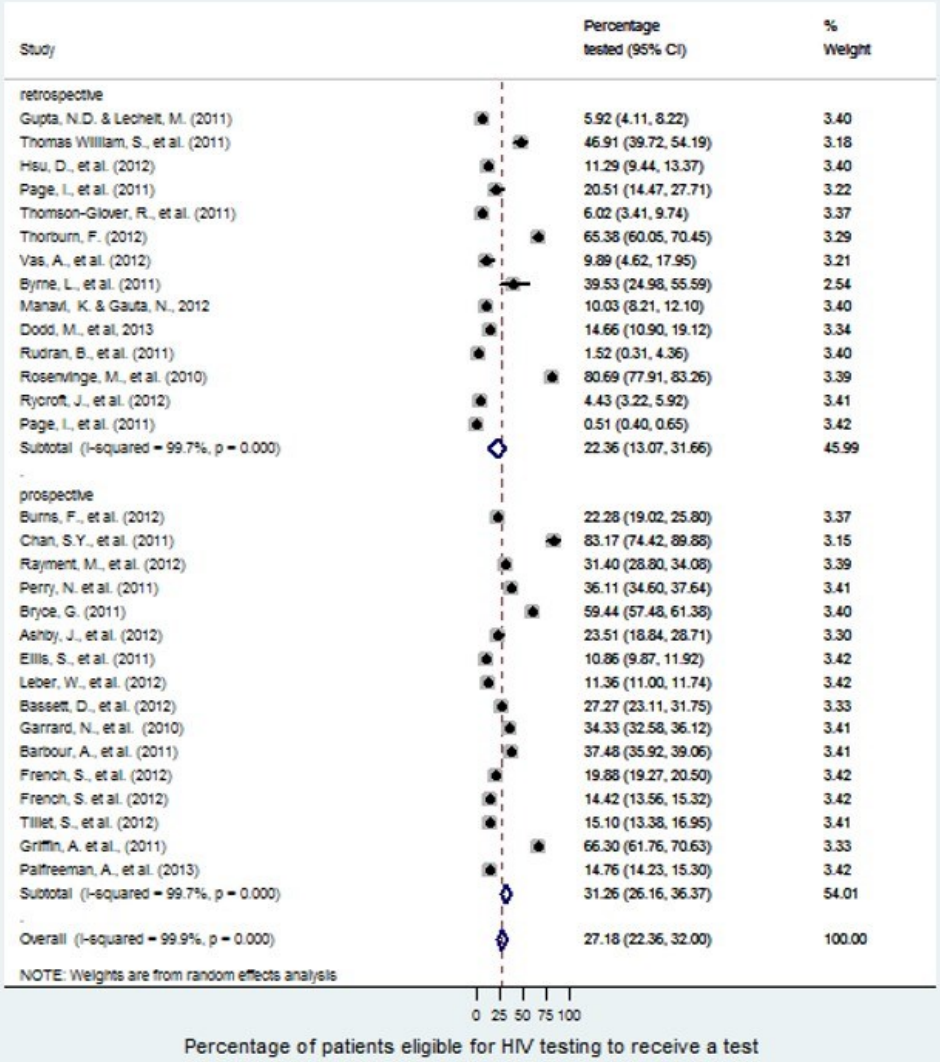


Figure 4f: Forest plot of test coverage by patient group

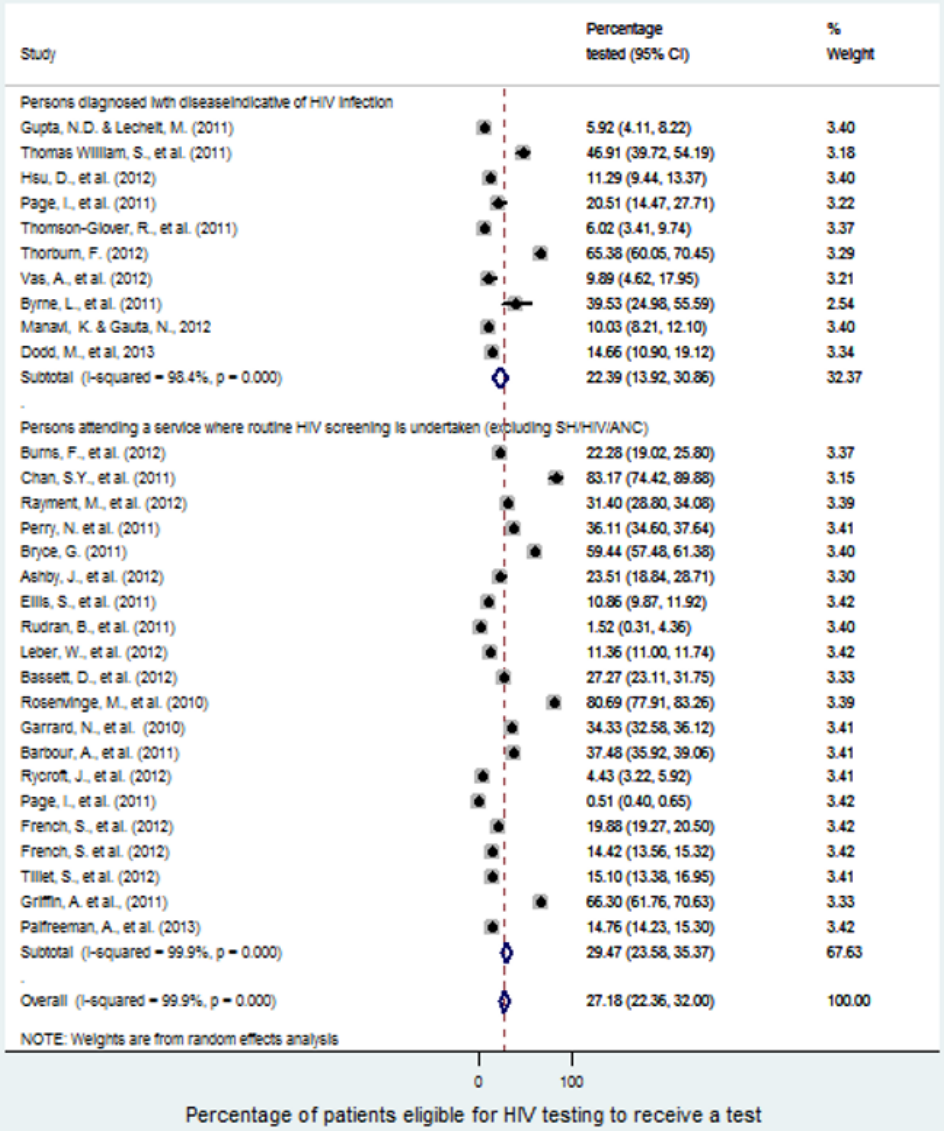
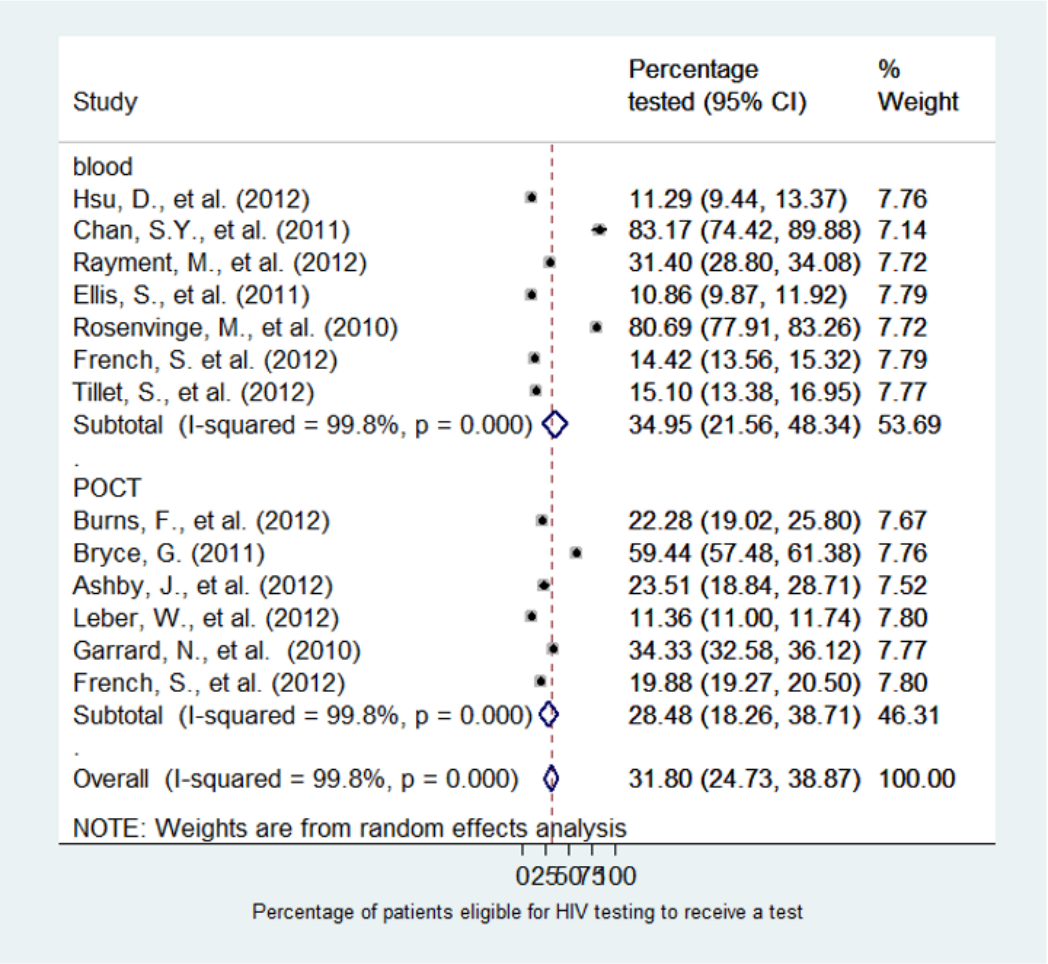


Figure 4g: Forest plot of test coverage by test type



There was considerable heterogeneity between studies included in all the meta-analyses with an I^2 value which varied from 99.7% to 99.9%. A meta-regression was undertaken to explore other study characteristics that may contribute to the heterogeneity and the results of this are presented in Table 4. A univariate analysis was undertaken for each covariate (including Patient Group, Test Type, Testing Strategy, Delivery Model and Study Location). None of these factors appeared to contribute significantly to the level of heterogeneity seen between studies. Results here should be interpreted with caution as many of the variables had small sample sizes; for example only three studies reported on the testing offered by HIV specialist staff.

In a univariate meta-regression model looking at Study Type in test coverage exclusively in persons attending screening settings (the only group to have both retrospective and prospective study types), Study Type was found to be a significant contributor to the level of heterogeneity seen in test coverage with an odds ratio of 6.6 (95% CI: 1.1%-39.77%) for receiving an HIV test in prospective studies compared to retrospective studies. As this was found to be significant at the 5% level the percentage of between-study variability explained by the covariate (R^2) was calculated. To calculate R^2, tau^2 for test coverage was calculated with no explanatory variable for studies undertaken in settings where HIV testing should be routine (2.81) and calculated for test coverage with Study Type as the explanatory variable (2.33). The adjusted R^2 for this meta-regression was 0.17, indicating that 17% of between study variance in the pooled estimate for coverage in studies of testing in patients attending setting where HIV testing should be routinely undertaken is due to Study Type. The result here should again be carefully interpreted as only 4 retrospective study types were used in the meta-regression for this patient group.

Covariate		N studies	OR (95% CI)	p-value
Patient group				
	Patients presenting with indicator disease conditions	10	1 (ref)	
	Persons attending screening settings	20	1.3 (0.4 - 4.3)	0.69
Location of study	London	14	1 (ref)	
	Non-London	16	0.5 (0.2 - 1.6)	0.24
Test Type	Point-of-care	6	1 (ref)	
	Laboratory	7	1.3 (0.3 – 7.1)	0.77
Delivery model*	Usual practice	18	1 (ref)	
	Staff education	9	1.4 (0.4 - 4.9)	0.59
	HIV specialist testing	3	3.6 (0.5 - 25)	0.18
Testing strategy	Opt-in	9	1 (ref)	
	Opt-out	12	1 (0.3 - 3.8)	0.99
Study Type	Retrospective	14	1 (ref)	
	Prospective	16	2.7(0.9 - 7.9)	0.07

* With only 3 studies in one of the categories, this result should be interpreted with caution due to lack of power

Table 4: Predictors of HIV testing level among eligible patients - meta-regression of results from studies identified, multivariate analysis

HIV test offer and uptake results

Table 5 shows the meta-analysis result for the percentage of eligible patients who were offered an HIV test across all studies reporting this information (n=14). For the forest plot of this meta-analysis and meta-analyses of percentage test offer stratified by Type of HIV Test, Testing Strategy, Delivery model, Location of study, Study type and Patient group, please see Appendix D: Forest plot for meta-analyses of percentage test offer a) overall and stratified by b) Test type b) Testing strategy c) Delivery model e) Location f) Study type and g) Patient group. The pooled estimate for overall HIV test offer is 40.48% (95%

CI: 24.3%-56.65%). As with overall test coverage, this was highest in Chan *et al.*, with 100% (95% CI: 96.41%-100%). Percentage test offer was lowest in Rudran *et al.* at 1.52% (0.3%-4.36%). When stratified by Patient group (Table 5), test offer is lower for patients diagnosed with an indicator disease condition at 9.25% (95% CI: 1.23%-17.27%) than for those attending screening settings, which was 45.51% (95% CI: 28.02%-63.01%). However, HIV test acceptance was higher in patients diagnosed with indicator disease conditions, at 87.4% (95% CI: 57.7%-100%) than in persons attending screening settings at 69.16% (95% CI: 52.74%-85.56%) Indicating that test offer is lower for patients with indicator diseases despite a higher test acceptance level in this group compared to persons attending screening settings. Overall HIV test acceptance was 71.45% (95% CI: 56%-86.89%) with the highest test acceptance level seen in Rudran *et al.* at 100% (95% CI: 29.24%, 100%) test acceptance and lowest in French *et al.* (2012) at 18.83% (95% CI: 17.3%-19.49%). There were however only 2 studies reporting HIV test offer or acceptance in patients diagnosed with indicator disease conditions.

HIV seropositivity levels

Of the total 30 studies included in the final analysis, 23 reported the number of those patients who tested positive for HIV and the meta-analysis results for the seropositivity observed in these studies is also presented in Table 5. For the forest plot for this meta-analysis and meta-analyses of percentage testing positive for HIV a) Patient group and b) Location please see Appendix E: Forest plot for meta-analysis of percentage testing positive for HIV a) overall and stratified by b) Location c) Patient group. The overall pooled estimate for percentage testing positive across all studies was 0.47% (95% CI: 0.28%-0.66%). When stratified by Patient group, pooled seropositivity was higher in patients diagnosed with an indicator disease at 2.71% (95% CI: 1.1%-4.36%) than those tested in screening settings 0.42% (95% CI: 0.25%-0.6%).

Patient Group	Percentage of those eligible who received HIV test (95% CI)	N studies	Percentage of those eligible who were offered HIV test (95% CI)	N studies	Percentage of those offered HIV test who accepted (95% CI)	N studies	Percentage of those tested who were HIV positive (95% CI)	N studies
Patients diagnosed with indicator disease	22.4% (13.9%-30.9%)	10	9.3% (1.2%-17.3%)	2	87.4% (57.7%-100%)	2	2.7% (1.1%-4.4%)	6
Persons attending screening settings	29.5% (23.6%-35.4%)	20	45.5% (28%-63%)	12	69.2% (52.7%-85.6%)	12	0.4% (0.2%-0.6%)	17
Overall	27.2% (22.4%–32 %) I^2 =99.9%	30	40.4% (24.3%-56.7%) I^2=100%	14	71.5% (50%-86.9%) I^2=99.8%	14	0.5% (0.3%-0.7%) I^2=51.5%	23

For test strategy and type of HIV test some studies were excluded from the sub-group analyses due to lack of data.

Table 5: Percentage of eligible patients who received HIV tests, percentages offered, accepted and HIV seropositivity in those tested: summary results from random effects model meta-analysis stratified by patient group

DISCUSSION

HIV test coverage in non-specialist clinical settings

The findings of this review indicate that the percentage of patients eligible for routine HIV testing in non-routine settings, as recommended by BHIVA/BASHH guidelines who receive a test is 27.18% (95% CI: 22.36%-32%). This low level of testing suggests that adherence to September 2008 UK guidelines for HIV testing is poor in the recommended populations and settings. Provider test offer to those eligible was estimated to be only 40.48% (95% CI: 24.3%-56.66%) whilst patient acceptance of testing was 71.45% (95% CI: 56%-86.9%). These results for test offer and acceptance levels suggests that the low overall level of testing is likely to be due to low levels of provider test offer and not patient acceptance. This trend of low provider test offer and high patient test acceptance has been seen in other countries in Europe and in the USA [84, 85] where it has been suggested that it indicates that health providers assess risk differently, are more likely to offer testing to patients they perceive to be at high risk or more likely to accept testing, with health care providers offering tests to people who they assess as being high-risk and those who are easier to approach with HIV testing. Aside from this, operational and training barriers such as inadequate training for routine test offer, lack of time or difficultly in ordering an HIV test have also been cited as barriers that may go towards reducing the level of health provider test offer.[86-88]

The highest levels of testing of the studies we identified were seen in Chan *et al.,* with 83.2% test coverage. In this study acceptability of consecutive HIV test offer in medical admissions in Croydon was assessed. A previous audit of HIV testing in this hospital showed that only 9/1047 patients had been tested for HIV. This indicates that consecutive test offer as undertaken in a prospective study such as this yields higher levels of test coverage than that seen in studies assessing routine data from audit. This is indeed seen as a factor that contributes significantly (p=0.04) to the variability seen in level of patient testing between studies when looking exclusively at screening settings such as this. This is only seen in this group however, and only 4 studies report audit results here for comparison. Additionally, other studies report high levels of testing, such as in Rosenvinge *et al.* with 80.7% test coverage present results taken from retrospectively collected data from screening settings and with no other covariates going to explain this variability in test coverage it makes it difficult to identify the factors that are truly contributing to higher test coverage seen in these settings.

Provider test offer and patient test uptake

Of those presenting with indicator disease conditions (including TB, glandular fever and other blood borne viruses), an estimated 22.39% (95% CI: 13.92%, 30.06%) received an HIV test compared to an estimated 29.18% (95% CI: 23.58%, 35.37%) of those attending screening settings where routine HIV testing should be undertaken. Although the odds of being tested for HIV if diagnosed with an indicator disease condition is not significantly lower than for those attending screening settings (0.8, p=0.67) this group represents a high risk population who are easily identified as so. Although there is little evidence regarding the prevalence of HIV infection in those of unknown HIV status presenting for care with such conditions, [89, 90] data from the USA and France indicated that delivering indicator disease guided testing in settings where this is a diagnosed HIV prevalence of 0.1%, is cost effective.[91-93] and testing in this patient group is a long-standing recommendation of national guidelines, even those prior to September 2008 and

HIV testing in indicator disease patients has been looked at in some depth with previous studies similarly finding low levels of testing for HIV in patients presenting with indicator disease conditions, including Read *et al.* who in 2011 found that 37% of patients newly diagnosed with HIV in their secondary care hospital had presented to healthcare services with an HIV indicator conditions in preceding 12 months but had not been tested at the time.[89] In a recent prospective study looking at the effectiveness of indicator condition-guided testing for HIV, *Sullivan et al.* found an HIV prevalence of 1.8% (95% CI: 1.42%-2.34%) across European centres, similar to our finding of an estimated seroprevalence of 2.7% (95% CI:1.1%-4.4%) in this group.[94] Furthermore, findings from an analysis from 13 counselling and testing sites in Italy indicated that those presenting late with HIV were probably already HIV positive at the time their initial indictor disease is diagnosed but that there is a median lapse of 22.6 months between indicator disease diagnosis and HIV diagnosis[95] and lack of adherence to guidelines in this group is likely to be hindering timely identification of HIV infection on a large scale.

HIV seroprevalence levels

A higher HIV seroprevalence was found in patients tested who presented with a disease indicative of HIV infection at 2.71% (95% CI: 1.05%-4.36%) than found in those tested in settings where routine HIV testing should be undertaken 0.42% (95% CI: 0.25- 0.6%) and the overall pooled seroprevalence from studies was found to be 0.47% (95% CI: 0.28%-0.66%). These seroprevalence estimates exceed the thresh-hold level 0.1% seropositivity of total tests administered deemed as cost-effective by CDC,[96]

indicating that HIV testing in these settings and populations is cost-effective and is likely to continue to be so with increased test coverage.

Limitations

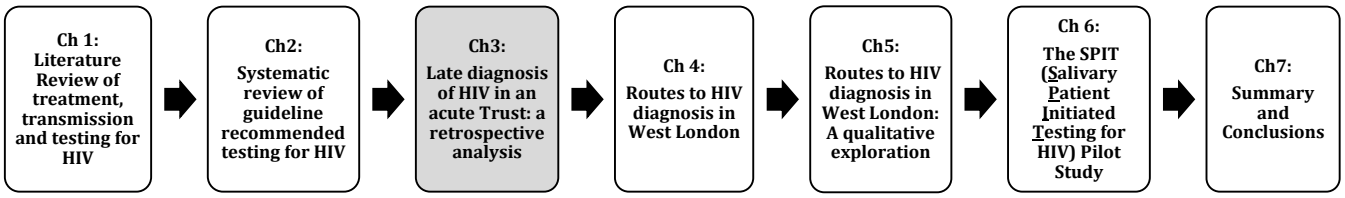
There are a number of limitations to this study, primarily the lack of a comparable routine data set with relevant information. Due to this there was reliance on a relatively small number of reports from local audits and studies that included a wide variety of populations, settings, duration and methods used for measuring HIV testing. However, as guideline recommendations are broad in their description of settings and populations, further restriction in inclusion criteria was not possible. The studies were of varied quality, and this could not be systematically assessed as many were published as reports or conference abstracts rather than peer reviewed papers. However the exclusion of low-quality studies did not have much of an impact on overall results (see Appendix F: Forest plot for meta-analysis of percentage testing positive for HIV a) overall b) by location c) by patient group). Data quality was also variable, with some dependent on patient self-report of previous tests to define eligibility. Several studies were interventional in nature, offering consecutive HIV tests in recommended settings and this may have contributed to an over-estimate of testing in routine conditions. However, these limitations could only be overcome through the implementation of standards for reporting in the context of some surveillance system such as those which already exist in established testing settings, such as ANC, SH/GUM.

There was a great deal of heterogeneity in the data with some I^2 statistic values at 100% and as a result caution should be taken in interpreting the summary statistics presented for illustration as an average proportion. True study percentages are likely to vary greatly around the estimate points presented. This is not a true level of overall test coverage level but rather an estimate from the data collected and a discussion to understand some of the variation which was associated with this. Although meta-regression did not identify any factor as a contributor to the between study variance seen, it is likely that much more of the heterogeneity could be explained by factors that could not be measured in the meta-regression either due to insufficient study numbers when or the fact that potential explanatory variables were not reported for all studies.

CONCLUSION

The results of this review and meta-analysis indicate adherence to 2008 national guidelines for HIV testing in the UK is poor and that low levels of provider test offer appears to be a major contributor to this, particularly in patients presenting with an indicator disease. Failure to adhere to testing guidelines is likely to be contributing to late diagnosis with implications for clinical outcomes and continued onwards transmission of HIV. Improved surveillance of HIV testing outside of specialist settings may be useful in increasing adherence to testing guidelines.

Chapter 3: Late diagnosis of HIV in an acute Trust: a retrospective analysis



As previously described, earlier diagnosis of HIV enables better treatment outcomes and reduces the risk of onward transmission. Additionally, current levels of HIV testing across the UK falls short of guideline recommendations and this is likely to be an important contributor to the fact that reductions in late diagnosis of those infected with HIV over the last decade have been modest.[68] In classifying stage of diagnosis, patients diagnosed with HIV in the UK are described in terms of their CD4 cell count at time of diagnosis with early diagnosis being at ≥350 cell/mm^3, late (the point after which ART should have been commenced) at <350 cells/mm^3. Stage of infection at the time of diagnosis with HIV is associated with a variety of demographic characteristics including ethnicity, age, sexuality and sex. Increased testing across a range of clinical settings is necessary for increasing earlier diagnosis in all patient groups however an exploration of the association of demographic characteristics and stage of presentation is an important step in understanding how and where HIV testing impacts on time of diagnosis of patients. In this chapter I will therefore explore the trends in HIV diagnosis amongst patients diagnosed with HIV within our Trust, exploring trends in demographics as well as any associations in location of diagnosis and stage of diagnosis.

INTRODUCTION

Late diagnosis of HIV in the UK

Although classifications for late diagnosis have changed in recent years, [124] there are common adverse outcomes that result from diagnosis of HIV infection at low CD4 cell counts. Those presenting with a CD4 cell count of <200 cells/mm^3 are, at increased risk of short-term morbidity, often resulting in a greater number of clinical events requiring hospitalization and an increased likelihood of complex

pharmacological therapy, which increases the risk of drug-drug interactions and overlapping toxicities.[125-126] These late presenters also experience lower rates of virological suppression and reduced CD4 cell count recovery on commencing ART in the first year of treatment compared to those diagnosed at higher cell counts [127-130] and as described in Chapter 1, late presenters also experience an increased risk of both short and long-term mortality. Due to a longer duration of undiagnosed infection, unmodified high risk behaviour and lack of viral suppressing treatment before diagnosis, late identification is an as important contributor to onwards transmission of HIV. For these reasons late HIV infection has also become a key indicator of the Public Health Outcomes Framework (3.04 – People presenting with HIV at a late stage of infection).[131]

Demographic Associations in Late diagnosis

The overall proportion of late diagnosis in the England is 48.3% and this is slightly lower in London at 44.9%.[132] Late presentation is however associated with being heterosexual, with 65% of heterosexual men and 57% of heterosexual women being diagnosed late compared to 35% MSM as seen for the year 2012 in Figure 1. Black African and Black Caribbean people are also at increased risk of late diagnosis with up to 61% diagnosed with HIV from these ethnic groups being diagnosed at a late stage of infection and there is a strong positive correlation with late diagnosis in HIV and increase in age, with figures from PHE indicating that the proportion of late diagnosis in people0 years old and older is 63% compared to the 44% seen in those younger than 50 years old.

These differences in time of identification with HIV are likely to be related to the differences seen in testing coverage between some of these groups. Data from SH clinics in 2012 indicate that this may indeed be the case with test coverage in MSM at 84% compared to 76% and 67% seen in heterosexual men and women respectively.[68] Despite the proportion of people being diagnosed late with HIV in the UK decreasing steadily and significantly over the last 4 years, as illustrated in Figure 1 this decrease continues with discrepancies in late diagnosis by risk group with >60% of heterosexual men being diagnosed late consistently from 2009-2012 compared to the 40%-34% late diagnosis seen in MSM.

Aim

The aim of this chapter is to explore the association of demographic factors, and location of testing with stage of disease at presentation for HIV in a West London Trust serving a diverse population. This is

achieved through a retrospective analysis of routine data including demographics, site of testing and CD4 count from all patients newly diagnosed with HIV in the five year period from January 2009 to December 2013.

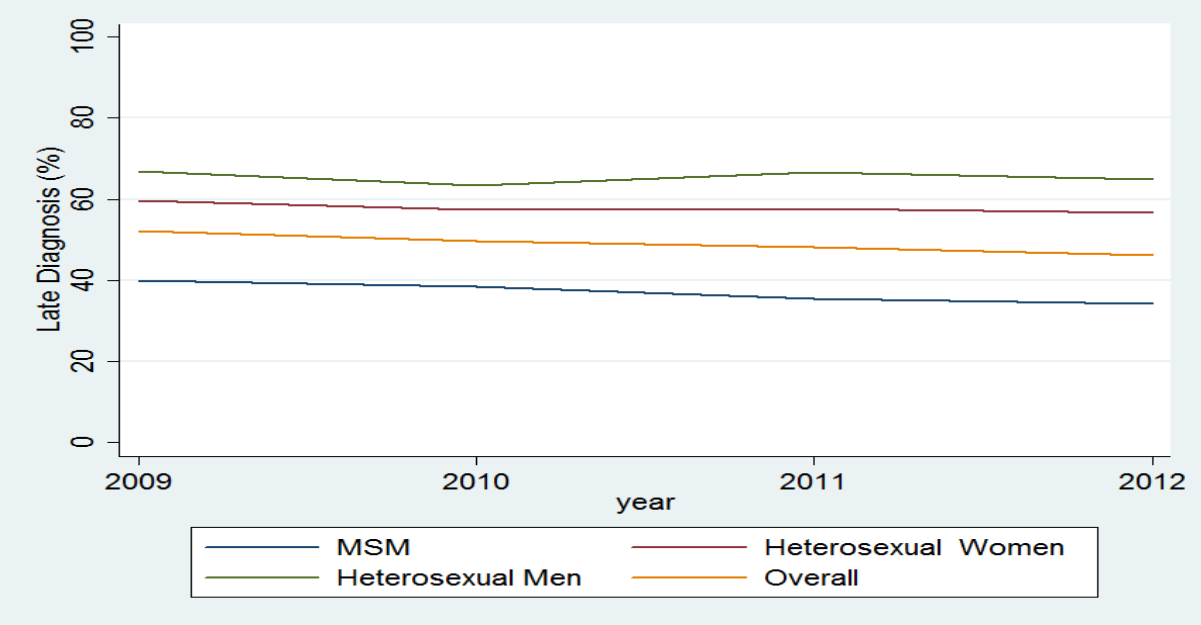


Figure 1: Proportion of adults diagnosed with a CD4 cell count of <350 cell/mm3 (within 3 months of diagnosis) by risk group from 2009-2012(data source PHE)

METHODS

Setting

Imperial College NHS Healthcare Trust (ICHT) is a large acute Trust in West London, providing specialist HIV services in an area with a high diagnosed HIV prevalence (>2 per 1,000 population of adults aged 15-59 years),[132] significant numbers of residents born outside the UK and a large proportion of these coming from countries with high national HIV prevalence. Data from the Survey Of Prevalent HIV Infection Diagnosed (SOPHID) indicate that the average proportion of late diagnosis in the three London Boroughs encompassing ICHT (Hammersmith and Fulham, Kensington and Chelsea and Westminster) ranges from 29.2% (24.2%-34.5%) in Westminster to 38.1% (30.9%-45.7%) in Kensington and Chelsea.

Data – Extraction, Cleaning and Coding

Data from all patients newly diagnosed with HIV within ICHT was obtained from the Jefferiss Wing, Sexual Health Clinic, St Mary's Hospital which manages HIV data for the whole Trust. The dataset is

routine in nature and used to ensure appropriate referral of patients newly diagnosed with HIV into the specialist HIV clinical service, first to the Clinical Nursing Specialist (HIV CNS) team and subsequently to HIV consultants for management. Although the database was created in 2001, complete information including CD4 cell count at diagnosis is only available from the start of January 2009; therefore this analysis includes all new diagnoses from those data until the end of December 2013. Variables within this database include: patient clinic number, date of birth, department source or location of referral, postcode, ethnicity, sexual orientation, name of consultant the patient is allocated to, first recorded CD4 cell count (recorded within two weeks from initial diagnosis). For this analysis date of birth, date of diagnosis, gender, ethnicity, sexual orientation, site of diagnosis and CD4 cell count at diagnosis was extracted.

Data were cleaned, coded and combined onto a single dataset using Microsoft Excel 2010. Cleaning involved the exclusion of patients without a CD4 cell count at diagnosis as this was used to infer stage of infection at diagnosis which is the key outcome variable for this analysis. Other exclusions included patients who were previously diagnosed with HIV and transferred their care from elsewhere, and neonates. Standardisation of definitions and description was also undertaken with ethnicity and location of diagnosis with individual nationalities being reclassified as ethnic groups (e.g. Indian or Pakistani reclassified as South Asian) and individual clinic names being reclassified as type of clinic (e.g. GUYS and Winsland to sexual health clinic). Additionally, due to a changes in database format from 2011, much cleaning involved standardising ethnicity classifications across all 5 years (See Appendix H: New variable codes in data analysis). All were initially recoded with specific subgroups being given individual codes and later re-coding conducted in Stata (see Appendix I for complete code) for broader analysis or increased stratification of different groups.

Statistical analysis

Outcome variables were created for late (CD4 <350 cells/mm^3) and non-late (CD4 ≥350 cells/mm^3) HIV diagnosis and a descriptive analysis was undertaken to illustrate what proportion of patients newly diagnosed were identified at a late stage and this was stratified by demographic characteristics including sex, sexual risk group, age group and ethnicity. Although the use of CD4 cell count as an indicator of late HIV diagnosis has limitations it continues to be a widely used tool for judging late diagnosis by clinicians and is the standard used for late diagnosis of HIV surveillance in the UK.[133-135] The key explanatory variables were demographic (including sex, age group and ethnicity) setting of diagnosis (either a

specialist testing setting or non-specialist) and time of diagnosis (early or late). Ethnicity was routinely recorded based on the National Ethnicity Code, which codes to a broad 'Group' such as White, Black and Asian and an additional 'Description' which specifies type of ethnicity (Complete code and description of ethnicity is in Appendix G). The category of Risk group is based on sexual risk group which is defined in routine data by patient sexuality, setting was defined as the clinical place where the test took place; these were then grouped into routine setting (diagnosis in a SH/GUM or ANC clinic) and non-routine (diagnosis elsewhere; including primary care, A&E or a medical or surgical admissions).

A regression model was then used to assess predictors of late presentation, generating both crude odds ratios and odds ratios adjusted for factors likely to impact on strength of association between dependent and independent variables. For example, the odds of late diagnosis in routine testing settings was compared to that in non-routine, with crude and adjusted confidence intervals also generated for these. The odds ratio of late diagnosis in 2009 was also compared to subsequent years to assess whether there had been a change in the proportion of late diagnosis of HIV. Clopper-Pearson 95% confidence intervals were generated for all odds ratios. Between group differences in stage of diagnosis was tested using a chi-square (χ^2) test for significance and were considered significant where $p < 0.05$. All data analysis was undertaken using STATA 12.0.

RESULTS

Patient characteristics

Patients diagnosed within the trust during the five-year period were aged between 13 and 77 years with a median age of 36 years (IQR: 28–43 years), with, the majority of new HIV diagnoses in the 25-39 age group. Over half (54%) of those newly diagnosed were White, 32.4% were Black (including Black African, Caribbean and British) and 11.1% Asian. Over 80% were men, and the majority of these (65.4%) fell under the category of MSM.

Most diagnoses were made in routine settings (494, 74.1%) 483, 70.6% were in sexual health clinics and 11 (1.6%) in ANC clinics. The remaining 186 (27.8%) were diagnosed in non-routine testing settings (20

in A&E, 138 in medical and surgical admissions, 14 in general practice and a further 14 in other non-routine settings).

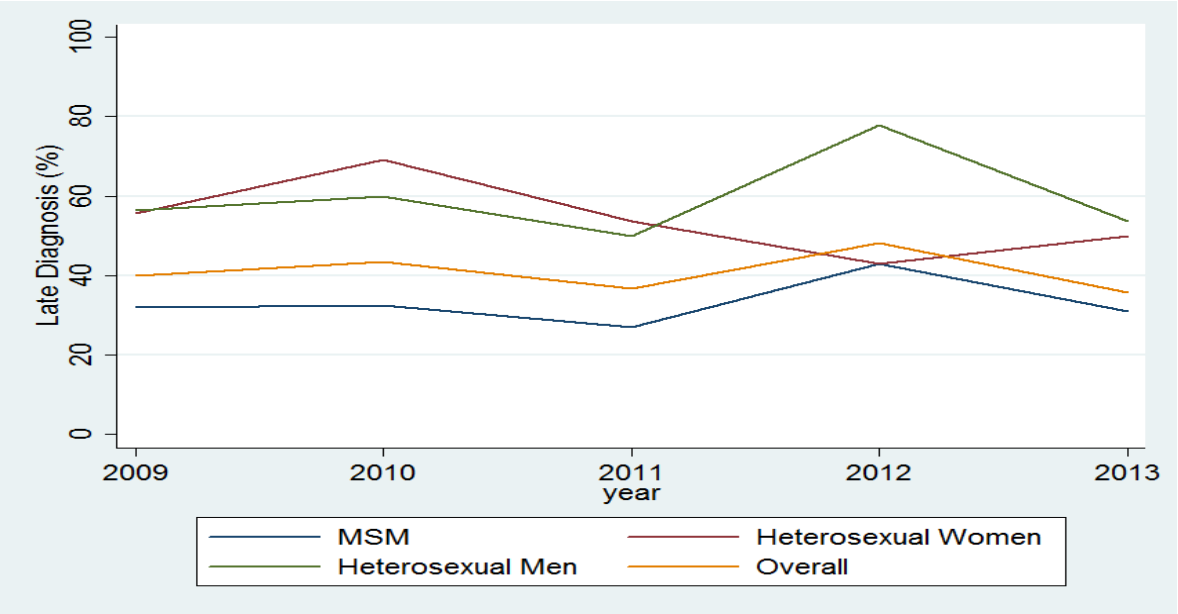


Figure 2: Proportion of ICHT patients diagnosed (within two weeks of diagnosis) with a CD4 cell count of <350 cell/mm3, by risk group from 2009 to 2013

Late diagnosis

Overall, 273 (40.1%) patients were diagnosed late, i.e. had a CD4 cell count of <350 cell/mm^3, with a majority having a CD4 cell count of ≥350 cells/mm^3 (394; 59.1%). Table one also shows the proportion diagnosed late by patient group. There is an increase in the proportion diagnosed late as age group increases with only 30.8% of those in the 15-24 group diagnosed late compared to 63.2% of those aged 50 years and over and stratified by ethnicity, the highest proportion of late diagnosis is seen in Black and the lowest is seen in White ethnicities (Table 1).

Figure 2 shows the percentage of patients diagnosed late over the 5 year period by risk group; for the period of 2009-2012 this was averages at 50.2%, lower than that of the national average of late diagnosis in this time period which was 53.8%. However, although nationally this figure has dropped from 58% to 47% in the last decade, the proportion of late diagnosis within ICHT has remained stable over the last 5 years. In this time period, the lowest percentage of late diagnosis is seen almost consistently in MSM over the 5 year period ranging from 27% in 2011 to 43% in 2012 compared to heterosexual men and women

and this pattern is similar to that seen in PHE data from the rest of England and Wales (Figure 1). In the ICHT data, unlike the PHE data, there is an increase in the percentage of late diagnosis in heterosexual women and a reduction in late diagnosis amongst heterosexual men from 2011, however neither of these observations were significant and we cannot be sure of their meaning due to the small number of heterosexual men and women diagnosed each year within the Trust, ranging from 18 at most heterosexual women in 2010 to 4 heterosexual men in 2012, at the lowest.

In a univariate analysis of the data, being diagnosed late was significantly associated with being female, >40 years of age, heterosexual and black compared to White and Asian groups (see Table 1). Following multivariate analysis, adjusting for ethnicity and age, being diagnosed late was not found to be significantly associated with being female and following adjustment for age, sex and sexual risk, being diagnosed late was also not found to be significantly associated with being Black, compared to White and Asian groups. However, after breaking down black ethnicity into Black African, Black Caribbean and black other, late diagnosis was found to be significantly associated with being Black African compared to other black ethnicities (Table 2) and this association remained significant following multivariate analysis adjusting for sex, sexual risk and age group.

	Number	**Diagnosed late (%)**	**Diagnosed late (CD4 cell count <350) OR (95% CI)**	**p-value**	**Diagnosed late (CD4 cell count <350) aOR* (95% CI)**	**p-value**
Sex						
Female (ref)	119	53 (44.5)	1		1	
Male	564	**339 (62.1)**	**0.5 (0.3 – 0.7)**	**<0.01**	0.6 (0.4 – 1)	0.07
Age group						
≥50 (ref)	95	60 (63.2)	1		1	
40-49	128	69 (53.9)	0.7 (0.4 – 1.2)	0.2	0.7 (0.4– 1.2)	0.2
25-39	350	116 (32.9)	**0.3 (0.2 – 0.5)**	**<0.01**	**0.3 (0.2 – 0.5)**	**<0.01**
15-24	94	29 (30.8)	**0.3 (0.1 -0.5)**	**<0.01**	**0.3 (0.2 – 0.6)**	**<0.01**
Ethnic group						
Black (ref)	162	88 (54.3)	1		1	
Asian	47	**14 (29.8)**	**0.4 (0.2 -0.7)**	**<0.01**	0.5 (0.2 – 1.1)	0.11
White	392	**131 (36.2)**	**0.5 (0.3 – 0.7)**	**<0.01**	0.8 (0.5 – 1.2)	0.29
Other	96	40 (14.7)	0.6 (0.4 – 1)	0.05	1 (0.5 – 1.7)	0.91
Sexual risk group						
MSM (ref)	436	143 (32.8)	1		1	
Heterosexual male	104	55 (58.9)	**2.5 (1.7 – 3.8)**	**<0.01**	**2 (1.2 – 3.2)**	**<0.01**
Heterosexual female	118	66 (55.9)	**2.9 (1.9 – 4.5)**	**<0.01**	**2 (1.2 – 3.3)**	**<0.01**
Other	9	5 (55.5)	**1.6 (0.4 – 6.2)**	**0.46**	1.3 (0.3 – 5.1)	0.75

Diagnosis location						
Routine screening setting (GUM/SH or Antenatal care clinic) (ref)	481	325 (67.7)	1		1	
Non-routine screening setting (including A&E, Acute medical admissions and general practice)	186	69 (37.1)	**3.5 (2.5 – 5)**	**<0.01**	**2.6 (1.8 - 3.8)**	**<0.01**

Table 1: Odds ratio for late diagnosis by demographic characteristics and testing setting

*Adjusted for age, ethnicity and sexual risk (where appropriate).

Ethnicity	**Diagnosed late (CD4 cell count <350) OR (95% CI)**	**p-value**	**Diagnosed late (CD4 cell count <350) aOR* (95% CI)**	**p-value**
Black African (ref)	1		1	
Black Caribbean	0.2 (0.07 -0.5)	<0.01	0.1 (0.05 – 0.4)	<0.01
Black Other	0.3 (0.1 – 0.8)	0.02	0.3 (0.1 – 1)	0.04
Asian	0.2 (0.1 – 0.5)	<0.01	0.3 (0.1 – 0.7)	<0.01
White	0.3 (0.2 -0.5)	<0.01	0.4 (0.3 – 0.8)	<0.01
Other	0.4 (0.2 – 0.7)	<0.01	10.6 (0.3 – 1)	0.07

Table 2: Odds ratio for late diagnosis by black ethnicities

Setting of diagnosis

Of the 186 diagnoses made in non-routine settings (including diagnoses made in A&E, acute medical admissions and general practice), 117 (62.9%) were in were patients with CD4 cell count of <350 cells/mm^3. Late diagnosis was significantly associated with being diagnosed in a non-routine HIV testing

setting compared to being diagnosed in routine HIV testing settings (including GUM/SH and ANC clinics) with the odds of late diagnosis in those diagnosed in routine settings being 3.5 (2.5 5) compared to those diagnosed in non-routine setting. This association remained significant following multivariate adjustment for sex, sexual risk, ethnicity and age group with odds of late diagnosis when diagnosed in non-routine settings being 2.6 (1.8–3.8) compared to those diagnosed in routine settings (as show in Table 1).

Figure 3 illustrates the percentage of those diagnosed late in routine and non-routine settings over the 5 year period from 2009–2013. Late diagnosis in routine settings ranged from 27.5% of total diagnoses made in 2011 to 35.9% in 2009 however in non-routine settings this ranged from 44.4% in 2011 to 77% in 2010. There is a consistently higher percentage of late diagnosis in non-routine setting compared to routine settings from year to year, this was only non-significant in 2013 (p=0.2).

The odds ratio of being diagnosed early in 2009 compared to 2013 was 1.2 (95% CI: 0.74–1.99) so there was no significant trend in proportion diagnosed late overall, or in the different settings. There was also no difference found in the change of the proportion of patients diagnosed late, in either routine settings (p=0.7) and non-routine settings (p=0.06) in the period from 2009 to 2013. The median CD4 cell count also remained stable from 420 cells/mm^3 (IQR: 188-640 cells/mm^3) in 2009 to 427 cells/mm^3 (IQR: 255-579 cells/mm^3) 2013.

Although the proportion of late diagnosis in routine settings did not decrease significantly in the period from 2009–2013, the percentage of all HIV diagnoses being made in these settings did increase significantly in this period; 21.5% in 2009, 25.4% in 2010, 25.9% in 2011, 38.8% in 2012 and 30.8% in 2013 (p=0.025).

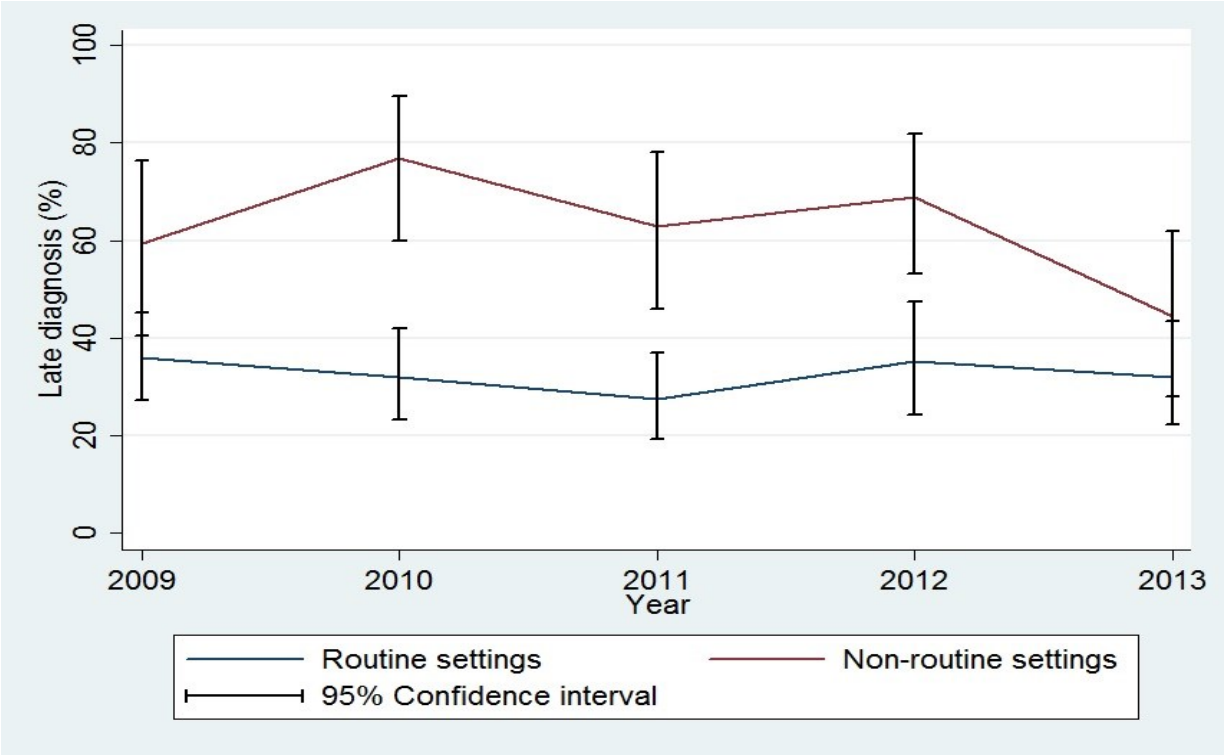


Figure 3: Percentage of patients diagnosed with CD4 cell count <350 cells/mm3 in non-routine testing settings, by year

Stage of Presentation (CD4 cell count at time of diagnosis)	2009 N, (%)	2010 N, (%)	2011 N, (%)	2012 N, (%)	2013 N, (%)	Total N, (%)
Early (≥350 cells/mm^3)	88 (59.1)	78 (56.5)	93 (63.3)	60 (51.7)	75 (64.1)	**394 (59.1)**
Late (< 350 cells/mm^3)	61 (40.9)	60 (43.5)	54 (36.7)	56 (21.6)	42 (35.9)	**273 (40.9)**

Table 3: Stage of presentation of patients diagnosed with HIV (Early and Late), by year

DISCUSSION

Late diagnosis

Findings from the results of this analysis show that within this Trust, there has been a smaller proportion of late (<350 cells/mm^3) diagnoses made compared to national figures, but this proportion has not reduced in the last five-years while this has been the trend nationally. This comparatively higher proportion of early diagnosis of HIV may be related to the demographic make-up of those attending the clinics within ICHT, with a number of dedicated gay men's sexual health clinic than in other parts of the country with convenient later opening hours, more patients falling into the risk category of MSM may be attending ICHT sexual health clinics so what may be shown is a reflection of the smaller proportion of late diagnosis seen in MSM and this may have resulted in a bias in those diagnosed with HIV within ICHT clinics. As the data from our clinics as well as national datasets[68] have shown, Black Africans are significantly more likely to be diagnosed at a later stage of infection and MSM are significantly more likely to be diagnosed at an earlier stage of infection than other groups. Higher rates of late diagnosis were seen in a similar audit undertaken in a south London hospital in the borough of Wandsworth[136] where they report that 40% of patients newly diagnosed with HIV were Black African, a higher proportion than the 18% seen in our clinics. Although authors do not provide a percentage of overall late diagnosis in the time period, they do provide median CD4 cell counts with an overall 240 cells/mm^3 compared to the median 410 cells/mm^3 (IQR: 210-591) seen in our clinics. It may however be that this difference is due to the

earlier time period that the data was taken from (2007–2011) in south London where CD4 cell counts were lower than in more recent years.

Despite the low comparative level of late diagnosis of HIV within ICHT, the data does not show that there has been an increase in early HIV diagnosis within ICHT, with no significant decrease in the percentage of those newly diagnosed being diagnosed with a CD4 cell count of <350 cell/mm^3. Whilst it appears that the majority of patients over the 5 year period were diagnosed before their CD4 count fell <350 cells/mm^3, over 40% of patients were not. This stability in the stage of presentation of patients diagnosed within ICHT does not correspond with national trends where there has been a significant reductions in the proportion of patients diagnosed late over a similar time period[68] or indeed compared to, other local clinical audits such as that conducted in South London where a 37% increase in median CD4 cell count at the time of diagnosis was observed from 2007-2011.[136]

The lack of a move towards earlier identification of HIV, despite increased testing initiatives has also been seen in many other centres and these findings within ICHT may be reflecting these. A systematic review and meta-regression of presented data describing the number or proportion of patients in CD4 cell count categories taken from 44 centres from Europe and North America indicate that mean CD4 cell count at presentation increased minimally from 307cells/μL in 1992 to 336 cells/μL in 2011.[137] Although the study incorporates many centres with varying populations and testing initiatives across the world, this finding of CD4 cell counts at first presentation not increasing meaningfully in developed countries is indicative of a stalling in the effectiveness of HIV testing strategies in some parts of the world and the need for a change in testing practice to improve this.

Associations of Late diagnosis

Late diagnosis appears to be independently associated with being heterosexual, diagnosis at an older age and being diagnosed in settings other than SH/GUM and ANC, which is similar to the findings of national audit data and other studies.[136,138-140] Our data suggests little improvement in these trends over the past three years. There have been great efforts towards increasing earlier identification of HIV infected people in the period in which these data were collected with changes in both national and local testing practices, including a move from serological to POCT testing and increased staff training for HIV testing in all departments. Despite this however, analysis of this data has not shown that this has resulted in a

significant reduction in the proportion of people diagnosed late within our trust and Black African populations continue to contribute disproportionately to late HIV diagnoses. What remains unclear however is to what extent the larger proportion of late diagnosis seen in Black Africans compared to other ethnic groups is due to low levels of testing as some evidence indicates that later presentation in Black Africans may not always be a reflection of the ability of local services to diagnose the infection but may be due to the fact that those diagnosed late have been in the country for a short period of time. In a cross sectional study undertaken by Burns *et al*. in a South London centre, it was found that the average length of time spent in the UK before HIV diagnosis for Africans was 36 months.[141] As information on time of migration is not routinely collected in our services, we could not assess whether there was any relationship between this and CD4 cell count at time of diagnosis in African or other migrants. However, as late presentation of HIV is commonly associated with symptoms of ill health, with these being the primary motive of individuals to seek healthcare, the likelihood is that diagnosis at an earlier point could have been a possibility and this is supported by findings such as those from 13 testing centres in Italy which indicate that those presenting late with HIV accessed services and received care an average of 22.6 months before being diagnosed with HIV[95] indicating that there are areas where increased testing could help reduce the proportion of late diagnosis in Black African ethnicities, particularly in those who access services in non-routine testing settings.[142]

Setting of diagnosis

The extent of HIV test administration is likely to be playing a part in the time of diagnosis of patients diagnosed within ICHT. Those diagnosed in non-routine testing settings were found to have an odds of 0.4 (0.3–0.5) of early diagnosis compared to those diagnosed in SH/GUM and ANC settings. It is quite likely that many other factors which distinguish patients attending and diagnosed in routine from non-routine testing settings may contribute to their stage of presentation. SH/GUM clinic attendees are more likely to be aware of their increased risk of HIV acquisition and may actively be taking the decision to test for HIV due to this knowledge (risk-based testing), whilst those admitted to medical and surgical departments are unwell and therefore more likely to have a lower CD4 cell count. However, many of the settings described as 'non-routine', including acute medical admissions and patients registering for primary care, are recommended HIV screening settings. This analysis illustrates that patients diagnosed in these settings

are diagnosed at significantly lower CD4 cell counts, indicating that an increase in routine testing may significantly contribute to the reduction of levels of late presentation of HIV within these settings.

Although we did not see a significant decrease in late diagnosis in either routine or non-routine settings we did see an increase in the overall percentage of diagnoses made in non-routine settings indicating that recent initiatives to increase HIV testing in a wider range of clinical settings appear to be having an impact. However, there is either not enough data collected as yet to see the impact of this on late diagnosis or the levels of late diagnosis are not likely to be affected by increased testing in non-routine settings and only a reduction in overall levels of undiagnosed HIV will be seen, which is unlikely to be the cause due to the increased proportion of late diagnosis in non-routine vs routine settings.

Limitations

This was a retrospective study of routinely collected clinical data and as such our analysis was constrained in some ways. Some information was missing, reducing the analysis to only 667 of the 715 cases that could potentially have been included. However, as this missing data is likely to be random, it is unlikely that this would have produced any systematic bias in the results seen but might have had an impact on our analyses by reducing power to detect differences between groups. Additionally, due to the way the data was collected (without indication of speciality in which diagnosis was made) it was not possible to differentiate the location of the new diagnosis made beyond the general descriptions of a routine or non-routine testing setting and incorporate an analysis of diagnosis by speciality. It is however unlikely that we would have enough large enough numbers diagnosed in each speciality to find significant differences in time of presentation and demographic differences in those diagnosed in these specialities. Much of what was identified in our demographic breakdown was similar to results from national datasets and other studies undertaken in London, [68, 132] indicating the relative reliability of the data extracted and the analysis undertaken.

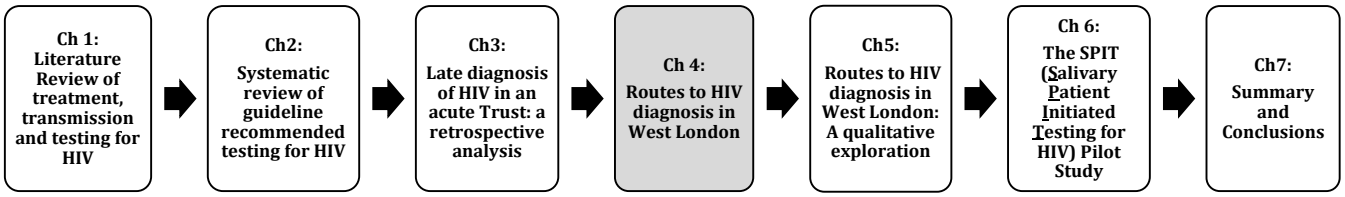
The demographic characteristics of those diagnosed with HIV at a late stage are similar to those seen in national audits and local audits in comparable parts of the country and these illustrate that the proportion of those being diagnosed later in infection has not reduced significantly despite changes in national and local guidance for HIV testing in this period. The difference in late presentation seen in SH/GUM and ANC compared to non-routine testing is large and may be an indication that expanded HIV

testing in recommended clinical settings is important in the reduction of late presentation of HIV in an area such as this.

CONCLUSION

These findings indicate that there is a need for more comprehensive HIV testing across non-routine HIV testing clinical settings in order to identify individuals before they present with late stage disease as medical emergencies. Further exploring the specific barriers to expanded testing for HIV is essential in reducing the undiagnosed fraction and proportion of late diagnosis of HIV in the UK.

Chapter 4: Routes to HIV diagnosis in West London



INTRODUCTION

In the previous chapter the demographic characteristics, stage and location of diagnosis of those diagnosed within a London Trust over a 5 year period was explored. When trying to gain an insight into patient routes to diagnosis however, descriptive characteristics and demographic associations have limited potential to identify the common paths that might explain the patterns seen in diagnosis or in identifying the obstacles to earlier diagnosis experienced by the patient. In this chapter, I will introduce a prospective study undertaken with those newly diagnosed with HIV within the ICHT over the period of a year. The study was undertaken to explore the routes patients take to diagnosis and additionally explore provider testing practices and obstacles to HIV testing. I will present only the results of the quantitative aspect of the study here. For results of the qualitative aspect of the study with presentation of results of semi-structured interviews please see Chapter 5 (Routes to HIV diagnosis in North West London: A qualitative exploration).

Aim

To explore routes to HIV diagnosis and factors contributing to testing for HIV in patients newly diagnosed with HIV in West London.

Objectives

1. To explore missed opportunities for earlier HIV testing in those diagnosed with HIV through investigator-led patient questionnaires.
2. To understand factors that contribute to HIV diagnosis using information gathered from semi-structured interviews.

METHODS

Setting and recruitment

We conducted an observational cross-sectional study of patients newly diagnosed with HIV at Imperial College Healthcare NHS Trust (ICHT) over a 12 month period from December 2012 to November 2013 (for the complete study protocol, please see Appendix J: Missed HIV study Protocol). Patients were eligible for participation if they were over 18 years of age, newly diagnosed with HIV in the above stated time period and assessed to be competent and suitable for participation by their doctor or nurse. Participant information sheets were offered to eligible patients after diagnosis and at least two further clinic attendances. Patients were asked to read the participant information sheet outlining the study and what they will be asked to do. The participant information sheet explained that all information given in the questionnaire was completely confidential, that patient participation is non-compulsory and that patient care will not be impacted upon in anyway by their decision to participate in the study or otherwise. Those agreeing to take part in the study signed a consent form (see Appendix L: Participant Information Sheet and Consent Form) and were then asked to complete the New HIV diagnosis questionnaire in the department or clinic they were being seen in along with the investigator. Patients were excluded from participation if they were under 18 years old or had previously been diagnosed with HIV elsewhere (i.e. transferred care) or had not attend > 2 clinical appointments with their doctor. In-patients were approached by the medical team in whose care they were under or by their CNS, with their questionnaire completion and interviews taking place during their hospital stay if their CNS and clinical team thought this acceptable.

Data were prospectively collected from newly diagnosed HIV patients with questionnaires (see Appendix K: Female and Male Questionnaire Template) capturing information relating to previous ill health, prior contact with healthcare services and testing history to assess and compare the routes to HIV diagnosis for late and early presenters within the trust. Where questionnaire completion was not possible, information was extracted from routine clinical data on basic patient demographic characteristics (including ethnicity, sex, sexuality and age), location of diagnosis, first recorded CD4 cell count, first recorded viral load, date of last negative HIV test and predicted country of infection for analysis.

Data analysis

For the quantitative analysis of the questionnaire results, descriptive statistical analysis was used to explore the demographic characteristics, risk profile and contact with health care services across all those patients newly diagnosed with HIV and between those presenting early and late with HIV infection. Comparison of the questionnaire response between those diagnosed at different stages in infection was made using chi-square tests (for categorical variables). A multiple regression model was used to adjust for the important variables where the reference category was early HIV diagnosis (CD4 >350 cells/mm^3). This analysis can be found in Appendix M: Complete STATA code for analysis of Missed HIV study data.

Ethical approval

Following application for Ethical Approval from the National Research Ethics Service (NRES) via the Integrated Research Application System (IRAS) and West London committee review, ethical approval was attained from both the NHS Research Ethics Committee and Research and Development within ICHT on 13/11/2012 (reference 12/LO/0779).

RESULTS

Over the course of the year 124 people were diagnosed with HIV and referred to St Mary's Hospital from within ICHT; of these 58 (46.8%) completed an investigator-led questionnaire. Of the remaining 66 participants; 34 (27.4%) were deemed not eligible to participate for 7 of these this was due to language barriers and lack of interpreter for the study (including 1 deaf patient), 2 were judged inappropriate for participation by their doctor and 1 was already aware of their HIV status and was receiving care elsewhere. Twenty-four patients who had been diagnosed with HIV during our study period were not eligible for recruitment as they had not had >2 consultant appointments during the study period. Thirty-two (25.8%) were eligible for participation. Of these 27 patients were not recruited due to recurrent appointment non-attendance (DNA) and 5 refused participation and declined to give a reason.

Newly diagnosed

From the routine data it is possible to describe demographic characteristics of all 124 patients diagnosed with HIV over the study period. The demographic breakdown of characteristics by stage of presentation is shown in Table 1: Characteristics of those diagnosed within the Trust from December 2012 to November 2013 by stage of presentation (n=124).

Viral load (log copies/ml) at diagnosis was available for 104 of the patients. A higher median viral load is seen in MSM compared to Heterosexuals, men compared to women and in the youngest age group (18–24 years of age) compared to older age groups. However, there was no difference in viral load between the early and late diagnosis groups and differences in viral load are not significant between any groups. Viral loads can be found in Appendix N: Median viral load and IQR for these patients, stratified by various demographic characteristics.

The majority of patients diagnosed over the course of the year were diagnosed in secondary healthcare settings. Seventy-five in SH/GUM clinic (60.5%), followed by 23 diagnoses as in-patients (18.6%) and 14 A&E (11.3%). This is a similar pattern of diagnosis as that seen in the 4 years preceding this period (see Chapter 3).

Information regarding whether a patient had ever before tested for HIV was available for 87 patients newly diagnosed with HIV and there were also some demographic associations seen in those having never tested for HIV, with black patients being significantly more likely to have never tested for HIV before being diagnosed than White patients and those 18-39 years of age being significantly more likely to have ever had an HIV test before their positive diagnosis compared to those 50 years and over. Men were also significantly more likely to have ever tested for HIV than women and heterosexuals significantly less likely than MSM with the unadjusted odds of never having had an HIV test are higher in heterosexuals compared to MSM; 5.1 (95% CI: 1.7-14.8), women compared to men; 6.8 (95% CI: 1.7-27.1) and black ethnicities compared to White ethnicities; 6.3 (95% CI: 1.8-22.2). However after adjusting for sex and sexual risk, the only demographic characteristic associated with having ever tested for HIV is being in the age group 18-39 years compared to those 50 years and over. This is presented in Table 3: Demographic characteristics and odds of never having been tested for HIV before positive diagnosis.

Characteristic	CD4 cell count at diagnosis		Total (%)
	<350 cells/mm^3 (%)	≥350 cells/mm^3 (%)	
Overall	**40 (32.3%)**	**84 (67.7%)**	**124**
Median CD4 cell count, cells/mm^3 (IQR)	150 (63-270)	551 (431-655)	423 (242-590)
Sex			
Female	9 (45)	11 (55)	20 (16.1)
Male	31 (29.8)	73 (70.2)	104 (83.9)
Ethnic group			
Black	10 (37)	17 (63)	27 (21.8)
Asian	2 (18.8)	9 (81.2)	11 (8.9)
White	23 (33.8)	45 (66.2)	68 (54.8)
Other/Unknown	5 (27.8)	13 (72.2)	18 (14.5)
Sexual risk			
MSM	23 (27.7)	60 (72.3)	83 (66.1)
Heterosexual Men	8 (38.1)	13 (61.9)	21 (16.9)
Heterosexual Women	9 (45)	11 (55)	20 (16.3)
Median Age, years (IQR)			
18-24	4 (28.6)	10 (71.4)	14 (11.3)
25-39	20 (29.4)	48 (70.6)	68 (54.8)
40-49	9 (32.1)	19 (67.9)	28 (22.6)
≥50	7 (50)	7 (50)	14 (11.3)
Location of diagnosis			
GUM/SH	15 (20)	60 (80)	75 (60.5)
ANC	1 (33.3)	2 (66.6)	3 (2.4)

In-patient department	12 (52.2)	11 (47.8)	23 (18.5)
A&E	8 (57.1)	6 (42.9)	14 (11.3)
GP	4 (66.6)	2 (33.3)	6 (4.8)
Other	0	3 (100)	3 (2.4)
Country of origin			
UK	22 (28.6)	55 (71.4)	77 (62.1)
Europe	0	8 (100)	8 (6.5)
Non-European	14 (66.6)	7 (33.3)	21 (16.9)
Unknown	4 (22.2)	14 (77.8)	18 (14.5)

Table 1: Characteristics of those diagnosed within the trust from 1st December 2012 to 1st December 2013 by stage of presentation (n=124)

The last date of a negative HIV test was available for 87 of those patients newly diagnosed with HIV in the study period. 20 patients (23%) reported never before having been tested for HIV. Of the remaining 67 (77%) who had tested in the past, the median time from their last negative test to their positive test was 8 months (IQR: 3.5-24 months). A total of 21 (31.9%) of those ever having tested for HIV had tested negative for HIV in the 6 month period before they were diagnosed. 20 of the 21 men in this group were categorised as MSM and 15 of these were White. None of the women in group had received a negative test in the 6 months before diagnosis and this indicates that the majority of those who had recently tested and therefore were recently diagnosed were White MSM, with no women being identified with recent HIV infection. Table 2 provides a breakdown of the proportion of those ever testing for HIV and those testing for HIV in the last 6 months by demographic characteristics.

Characteristic	Test ever for HIV (n=87)		Date of last negative test (n=67)	
	Ever tested (%)	**Never tested (%)**	**<6 months ago**	**≥6 months ago**
Overall	**67 (77%)**	**20 (23%)**	**21 (31.3%)**	**46 (68.7%)**
Median CD4 cell count, cells/mm^3 (IQR)	514 (360 – 616)	226.5 (145 – 547)	551 (467 – 7110)	470 (270 – 600)
Sex				
Female	4 (40)	6 (60)	0	4 (100)
Male	63 (81.8)	14 (18.2)	21 (31.3)	42 (62.7)
Ethnic group				
Black	7 (46.7)	8 (53.3)	3 (42.9)	4 (57.1)
Asian	6 (85.7)	1 (14.3)	0	6 (100)
White	44 (84.6)	8 (15.4)	15 (34.1)	29 (65.9)
Other/Unknown	10 (76.9)	3 (23.1)	3 (30)	7(70)
Sexual risk				
MSM	54 (96.4)	2 (3.6)	20 (37)	34 (63)
Heterosexual Men	9 (42.9)	12 (57.1)	1 (11.1)	8 (88.9)
Heterosexual Women	4 (40)	6 (60)	0	4(100)
Median Age, years (IQR)				
18-24	10 (83.3)	2 (16.7)	5 (50)	5(50)
25-39	40 (85.1)	7 (14.9)	14 (35)	26 (65)
40-49	13 (72.2)	5 (27.8)	2 (15.4)	11 (84.6)
≥50	4 (40)	6 (60)	0	4 (100)
Location of diagnosis				
GUM/SH	47 (83.9)	9 (16.1)	17 (36.1)	30 (63.8)
ANC	1 (100)	0	0	1 (100)

In-patient department	9 (52.9)	8 (47.1)	2 (22.2)	7 (77.8)
A&E	4 (57.1)	3 (42.9)	2 (50)	2 (50)
GP	4 (100)	0	0	4 (100)
Other	2 (100)	0	0	2 (100)
Country of origin				
UK	57 (85.1)	10 (14.9)	19 (33.3)	38 (66.6)
Europe	5 (83.3)	1 (16.6)	1 (20)	4 (80)
Non-European	5 (35.7)	9 (64.3)	1 (20)	4 (80)

Table 2: Proportion of those ever testing for HIV and testing for HIV in 6 months before diagnosis by demographic characteristics

Questionnaire results

Those completing the new diagnosis questionnaire were largely demographically representative of the total patients newly diagnosed with HIV over the study year period with median age being 33 years (IQR: 27–45 years) and 52 (56.9%) from White ethnic group, 7 (10.3%) from Asian ethnic groups, 15 (15.5%) from black ethnic groups and 13 (17.2%), unknown or other ethnic groups. There was however under sampling of women with 53 (91%) of those completing investigator led questionnaire being male and some under sampling of heterosexuals, with only 16 (27.6%) falling into this group. 16 (27.6%) of those completing the questionnaire were UK born, with a further 12 (20.7%) being born in Europe and 30 (51.7%) born outside of Europe. Of those born outside of Europe however, the median time spent living in the UK was 7.5 years (IQR: 4-15 years) indicating that individuals diagnosed with HIV but coming from outside of Europe, have been living in the UK for several years before HIV diagnosis.

Demographic Characteristic	**Odds of having ever tested for HIV (95% confidence interval)**	**p-value**	**aOR* of having ever tested for HIV (95% confidence interval)**	**P-value**
Ethnicity				
White	1 (ref)		1 (ref)	
Asian	1.1 (0.1-10.3)	0.9	1.3 (0.1-14)	0.8
Black	**0.2 (0.05-0.56)**	**<0.01**	0.3 (0.7-1.3)	0.1
Other/Unknown	0.6 (0.1-2.7)	0.5	0.8 (0.2-3.9)	0.8
Age (years)				
≥ 50	1 (ref)		1 (ref)	
40-49	3.9 (0.8-19.9)	0.1	5.0 (0.8-29.4)	0.07
25-39	**8.6 (1.9-38.3)**	**<0.01**	**8.8 (1.8-42.7)**	**<0.01**
18-24	**7.5 (1-54.1)**	**0.05**	**12.7 (1.2-13)**	**0.03**
Sex				
Female	1 (ref)		1 (ref)	
Male	**6.8 (1.7-27.1)**	**<0.01**	2.7 (0.5-14.3)	0.2
Sexual risk				
MSM	1 (ref)		1 (ref)	
Heterosexual	**0.2 (0.1-0.6)**	**<0.01**	0.3 (0.4-13.6)	0.4

*Adjusted for sex and sexual risk

Table 3: Demographic characteristics and odds of never having tested for HIV before positive diagnosis (n=87)

HIV testing

Among the 58 individuals completing the questionnaire, 17 (29.8%) reported never having tested for HIV and of those testing at least once for HIV, the median time from last negative test was 9.6 months (IQR: 5.5–35.5). Thirty (73.2%) of these tests were taken at a GUM/SH clinic, with 4 (9.8%) being taken with a GP and 1 at an A&E. Six (14.6%) of the tests were taken in 'other' locations, including private primary care clinics or as part of company health screens. Twenty-six (63.4%) of those completing the questionnaire reported that they had actively gone to seek an HIV test when they were last tested with the remaining proportion reporting that the testing was prompted solely by a doctor or nurse. 8 patients had ever refused HIV testing in the past and reasons for this were related to fear, with 3 citing this as a reason for test refusal and the remaining four stating issues related to low risk perception, however only one stated a recent HIV test as a reason for test refusal. All of those having refused an HIV test at some point in time had previously tested for HIV, indicating that those who had never tested for HIV never sought out an HIV test or were never offered.

HIV exposure and sexual risk

Thirty-six (62.1%) of those completing the questionnaire had ever been diagnosed with an STI, including chlamydia, gonorrhoea, herpes and syphilis. However, the date of last STI diagnosis was variable with a median 17.7 months (1.3- 47.8 months). Three patients had reported being given PEP (Post exposure prophylaxis) following a suspected HIV exposure and all of these had received HIV negative test results subsequent to PEP use. A further three patients had also reported ever having a blood transfusion, however only two patients were able to provide a date for a negative HIV test subsequent to the transfusion date. Two patients had reported previous injecting drug use, one of whom also reported needle sharing, and this patient had also never tested for HIV before their positive diagnosis. Overall however, there was no association found between use of PEP, receiving a blood transfusion, injecting drug use/needle sharing and having ever tested for HIV before diagnosis and too few participants reporting these risk factors were identified for a formal analysis to be undertaken.

Eighty-five percent of MSM reported sex with a causal partner in the 6 months before diagnosis, with a median number of 3.5 partners (IQR: 2-7) and 64 (75%) of these men also reported unprotected sex with these casual partners. Fifteen (7.1%) of all those reporting sex with a casual partner were aware of a positive HIV status of these partners with 63 (74.3%) unaware of a casual partner's HIV status. Only five

heterosexual women completed the questionnaire and 3 reported sexual intercourse with 1 casual partner in this period and two of these reported that this sex was unprotected. One of these women was also aware of the HIV positive status of her partner. 11 heterosexual men completed the questionnaire and 6 of these reported sex with a casual sexual partner in the 6 months before diagnosis. The number of sexual partners reported in this period was variable among heterosexual men, ranging from 2 to 15. All reported unprotected sex with at least one of these partners and none were aware of the HIV status of those partners. There was no significant association found between having a casual sexual partner, having a known HIV positive partner, having a sexual partner who is born in a country of high HIV prevalence in the 12 months before HIV diagnosis and having an HIV test in that time period. There was also no association found between the total numbers of unprotected casual sexual partners in the last 6 months and testing for HIV in the last 6 months. This indicates that recent high-risk sexual behaviour in itself did not prompt HIV testing in this group.

Contact with Health care Services

In assessing previous ill health among those completing the new diagnosis questionnaire, it was found that 42 (73.7%) of those newly diagnosed with HIV had felt unwell in the 12 months prior to being diagnosed with 39 (67.2%) of these seeking some form of healthcare for this; 20 (34.5%) first went to visit their GP and13 (22.4%) first went to a SH clinic. One went directly to A&E at first symptom of ill health and 5 chose to first go to a pharmacy or drug store to seek advice or to self-prescribe. Table 4 provides a breakdown of the proportion of those seeking health care by demographic characteristics at first instance of ill health.

Symptoms experienced in the year preceding diagnosis were variable. Of the 39 patients experiencing symptoms and visiting a healthcare service for this, the majority reported coughing, fever and fatigue and a large proportion also reported gastric symptoms such as diarrhoea, nausea and vomiting. Symptoms reported were highly diverse however with some patients having only visited their doctor with neurological symptoms, recurrent UTI (urinary tract infection) or lymphadenopathy with no other symptoms. One patient was admitted to AMU only once in the year before HIV diagnosis for a dislocated jaw and cuts to the head, unrelated to HIV infection.

Twenty-six of the 39 (66.7%) were not tested for HIV in the 12 months prior to HIV diagnosis despite the fact that 17 (29.3%) went for a return visit to their GP, attended A&E or were admitted to an AMU after a second incident of ill health or when their symptoms did not resolve and in total 13 (22.4%) of those completing the new diagnosis questionnaire visited a health care service more than twice in the 12 months before being diagnosed without being offered an HIV test. This is illustrated in Figure 1. It is unclear the total length of time participants completing the questionnaire had symptoms and were visiting a health service for as the questionnaire only specified instances of ill health in the 12 months before diagnosis, with the possibility of many participants experiencing periods of ill health before this time that was not recorded.

Forty-eight (82.8%) of those diagnosed with HIV in the study period were registered with a GP and the median period of time that they had been registered with their current GP was 4 years (IQR: 1.5–11 years) and 46 (79.3%) of all patients completing the questionnaire reported visiting their GP at least once in the year before they were diagnosed and not being offered an HIV test at their primary care clinic. There was however no association between the setting (GP, A&E or AMU) attended with symptoms of ill health (and indicative of HIV infection) in the 12 months preceding their HIV diagnosis and the odds of being offered an HIV test in patients presenting to A&E or being admitted to AMU compared to those presenting to their GP being 2.7 (95% CI: 0.5-14.4), p= 0.24.

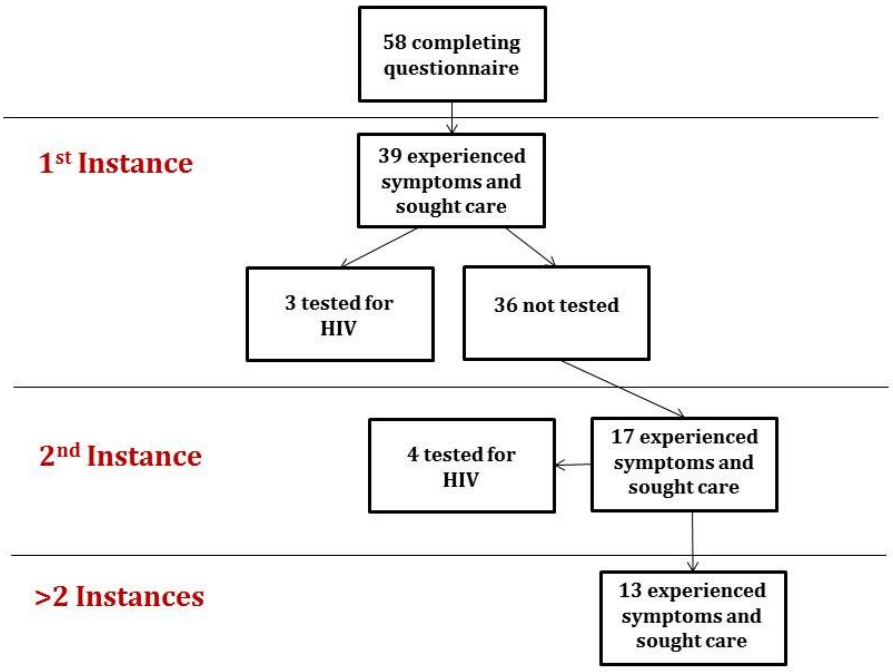


Figure 1: Flow diagram of patients experiencing symptoms indicative of HIV infection, whether they sought care and whether they were tested

Characteristic	Health care sought at first instance of ill health in the 12 months before diagnosis			
	GP visit	GUM/SH clinic visit	Other (A&E and Pharmacy)	Total (%)
Overall	**20 (51.3%)**	**13 (33.3%)**	**6 (15.4%)**	**39**
Sex				
Female	0	3 (75)	1 (25)	4 (10.3)
Male	20 (57.1)	10 (28.6)	5 (14.3)	35 (89.7)
Ethnic group				
Black	2 (25)	5(62.5)	1 (12.5)	8 (20.5)
Asian	2 (66.6)	1(33.3)	0	3 (7.7)
White	13 (62)	4 (19)	4 (19)	21 (53.8)
Other/Unknown	3 (42.9)	3 (42.9)	1 (14.2)	7 (17.9)
Sexual risk				
MSM	15 (60)	7 (28)	3 (12)	25 (64.1)
Heterosexual Men	5 (50)	3 (30)	1 (10)	10 (25.6)
Heterosexual Women	0	3 (75)	1 (25)	4 (10.3)
Median Age, years (IQR)				
18-24	4 (57.1)	2 (28.6)	1 (14.3)	7 (18)
25-39	9 (56.3)	4 (25)	3 (18.8)	16 (41)
40-49	3 (37.5)	3 (37.5)	2 (25)	8 (20.5)
≥50	4 (50)	4 (50)	0	8 (20.5)

Table 4: Proportion seeking health care at first instance of ill health in the 12 months before diagnosis by demographic characteristics

Recent migration and stage of diagnosis

As described in previous chapters (Chapter 1 and Chapter 3), other studies in the UK, USA and Europe, and PHE data, illustrate that late diagnosis of HIV is strongly associated with Black (and particularly Black African) ethnicity. Investigations into why this may be the case has led to studies exploring barriers to HIV testing and general health service access in these ethnic groups, with recent migration being cited as a cause for late diagnosis. 42 were identified and 9 of these were patients of Black African ethnicity who reported being born abroad and completing the questionnaire, the average period of residence in the UK was 12 years (IQR:7-13 years), all of these patients had a CD4 cell count <350 cells/mm^3 at the time of their HIV diagnosis and only 2 reported having ever tested for HIV in the past, despite the majority presenting to their GP, A&E or being admitted to AMU at some point in the 12 months before they were diagnosed with HIV. The number of patients of Black African ethnicity, completing the questionnaire and reporting being born abroad was too small to assess whether there was any association in duration of residence in the UK and risk of being diagnosed late with HIV, however, across the entire sample of those completing the questionnaire and reporting being born abroad (n=42), there was no association found between late diagnosis and duration of residence in the UK; the odds of late diagnosis (CD4 cell count <350 cells/mm3) was 0.7 (95% CI: 0.1-3.7) and 0.6 (95% CI: 0.1-2.7) in those living in the UK for 5-10 years and >10 years respectively, compared to those living in the UK for <5 years. Although the sample is not powered to detect this difference and there is a risk of response bias in the time reported as living in the UK, there was no association found between recency of migration and stage of HIV diagnosis in this group.

DISCUSSION

The results of the quantitative analysis of the data taken from those diagnosed with HIV within the trust over the yearlong study period have shown that ever having tested for HIV before diagnosis, regular HIV testing (more than once a year) and earlier diagnosis continues to be strongly associated with young MSM. Findings also indicate a lack of association between sexual risk behaviour and HIV testing as there was no significant association identified in reported number of casual sexual partners, instances of unprotected sex and even awareness of HIV status of partner in the 6 month period before diagnosis and number of HIV tests taken. This coupled with the finding that patients never testing for HIV have never refused a test offer and that only a third of patients presenting to health providers (at a primary or

secondary health care service) are diagnosed within a year appear to be strong indicators of the importance of the role of the health provider in initiating testing.

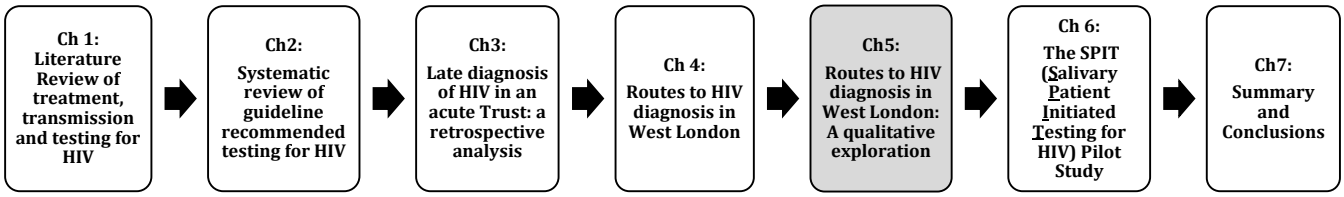
low participation rate in this study is likely to have biased our findings, and the under representation of heterosexuals and those from other non-White ethnicities compared to White gay men is an indication that those participating were not wholly representative of the clinic population. This was further compounded by the difficulty in finding a translator for both the questionnaire and interview aspect of the study for some patients, which is likely to have further biased our sample toward UK born, English speaking patients. Despite this bias in recruitment, the study was prospective in its recruitment of patients and comprehensive in its assessment of individual routes to HIV diagnosis.

Although BASHH/BHIVA guidelines recommend routine HIV testing in general practice only in those newly registering with a GP almost 90% of participants reported being registered with a GP at the time of their diagnosis with HIV and most of these had been registered with their GP for several years, so routine testing of new registrants would not have resulted in earlier diagnosis of these patients. Results from the analysis indicated that there is no significant difference in probability of test offer in those attending their GP with symptoms indicative of HIV infection and those visiting settings such as A&E or on admission to AMU.

CONCLUSION

Results from this analysis of patients newly diagnosed with HIV within our Trust offers interesting findings related to patterns of testing for HIV, particularly regular HIV testing (and early HIV diagnosis) continuing to be strongly associated with SH/GUM clinic attendance, which is associated with young MSM, a lack of provider initiated testing in other settings and a lack of correlation with testing in patients with higher sexual risk behaviours. In the following chapter these findings will be explored in depth through participant interviews in order to better understand the reasons for the patterns identified here.

Chapter 5: Routes to HIV diagnosis in West London: A qualitative exploration



Chapter 4 describes the findings of the patient questionnaires undertaken to assess patient routes to HIV diagnosis. Analysis of the questionnaire alongside routine clinic data indicate that demographic characteristics and timing of HIV diagnosis are much like those seen in patients diagnosed with HIV within the trust in previous years (Chapter 3). The majority of patients diagnosed over the 12 month course of the study (68%) had a CD4 cell count ≥350 cells/mm^3, with the majority of these patients being younger (91% <49 years), White (54%) and categorised as MSM (71%).

In addition to this, the questionnaire also provided information on patient HIV testing history and practices, ill health and contact with health services in the year prior to diagnosis, and HIV exposure history and sexual risk behaviour, with findings indicating that when testing was undertaken it was a regular occurrence with the median time since last HIV negative test in the group being 8 months (IQR: 3.5-24 months). After adjusting for sex and sexuality the only demographic characteristic associated with never having been tested for HIV is being aged 50 years or older and all participants indicating they had never received an HIV test also indicated that they had never refused a test. Importantly, there appeared to be a lack of correlation in patient risk of HIV exposure or high-risk sexual behaviour, and HIV testing frequency.

These findings raise questions relating to patient ideas of HIV testing and how their understanding of risks, their own health and the health services available to them may impact on this, which will be explored qualitatively in this chapter.

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

INTRODUCTION

Previous studies conducted in the UK and Europe have provided useful findings relating to the barriers that exist to ever having tested, and increased or regular testing for HIV. In a review undertaken on Barriers to HIV testing in Europe, [84] barriers are classified into three categories; 'Institutional/Policy level', 'Healthcare provider level' and 'Client/Patient level'. Although this classification is useful in characterising key common elements identified across groups such as risk perception, fear of diagnosis and disclosure, and accessibility of health services, there is little exploration of how these themes vary between different groups which is important in explaining the discrepancies between groups that have been identified in the previous chapter. An important element in HIV testing identified in the review was the variation in the level of normalisation of testing for HIV throughout Europe and the tendency towards largely selective testing, which has also been identified in the UK (Chapter 2) and making its findings more translatable to the UK.

Low risk perception as a barrier to HIV testing has also been identified in other studies reporting on questionnaire results from several European countries (France, Estonia, Portugal and Finland) [143, 144] amongst those at risk of HIV infection or recently diagnosed with HIV. In a cross-European questionnaire of patients newly diagnosed with HIV, it was found that the most frequently reported reason for prompting an HIV test was a worry about a risk exposure with 214 (34%) participants citing this as a prompt for testing. However, amongst participants whose first ever HIV test was positive, low risk perception (73%) was the most frequently cited reason for never having tested.[144] The lack of correlation in risk of HIV exposure and testing practice was also identified amongst ICHT patients in the previous chapter and when this occurs against a back drop of more selective over normalised testing for HIV, as is widely seen throughout Europe[84] it is a barrier which may be an important contributor to late identification of HIV in the UK. Low risk perception was also identified as a major contributor to late diagnosis in France[145] within a large cohort of HIV infected patients where those identifying as low-risk for HIV infection were at high risk of late detection. It is clear therefore that some findings from the patients participating in the Missed HIV study are similar to those seen elsewhere and an exploration of HIV positive patients' ideas and attitudes towards HIV testing is of importance in elucidating the reasons for this.

Aim

To better understand the findings from the Missed HIV questionnaire through a qualitative exploration of impact of the perceived risk, ill health and health practices on HIV testing behaviour among recently diagnosed HIV positive patients.

METHODS

Participants and Recruitment

Patients recruited to and completing a questionnaire as part of the Missed HIV study were eligible for participation in the qualitative aspect of the study. A purposive sampling method was employed for the identification of eligible patients for interview. All participants completing the questionnaire aspect of the study were asked if they would be willing to participate in a semi-structured interview exploring issues related to the answers they provided in the questionnaire. Participants agreeing to interview were sampled according to demographic characteristics such as gender, age and ethnicity in order to include a representative cross-section in of those completing the questionnaire. Participants were interviewed directly after completing the questionnaire by the same researcher and where this was not possible, invited for interview at their next clinical attendance (complete recruitment method is available in Appendix J: Protocol for Missed HIV Study). In order to reduce selection bias, not all participants agreeing to interview were invited to complete one, ensuring the interview sample was representative of our questionnaire sample.

Topic guide and Interview

The semi-structured interviews undertaken were to be 30 minutes to an hour in duration. The interviews were interactive, with topics covered relating broadly to the participant attitude to HIV/AIDS, ideas around healthcare services and healthcare providers in the context of testing for HIV (the complete topic guide is available as Appendix O: Missed HIV Participant Topic Guide). Before commencing the interview, participants were informed that the interview would be audio recorded on a small device (using an Olympus DM-450 Dictaphone), that the audio tape would be transcribed for analysis with identifiers (including names and addresses) removed and subsequent to this, that audio recordings would be permanently deleted.

All interviews were audio recorded and subsequently independently transcribed verbatim by another party, with the exception of two interviews undertaken in Arabic, where the researcher conducting the interviews, translated and transcribed the audio material.

An iterative process of interviewing was employed in order to refine the data collected to areas of interest for analysis. The first 6 interviews were reviewed and key themes were identified and used to guide further interviews and once these themes became clear (data saturation in a given area was complete), they were explored in less detail in later interviews. In practice this meant that questions incorporated in the Topic Guide were not all used in later interviews and that the questions posed in these interviews were refined to elicit content related to themes still to be explored. Notes relating to the setting, describing the patient and their demeanour as well as any notable activity within the clinic relating to the patient and the interview were recorded following the interview by the researcher. These notes were added to transcribed interviews as a memory aid and provided a description which put each transcript into context during analysis.

Data Analysis – Framework Analysis

Analysis of the transcripts was undertaken using the Framework analysis method. This is a thematic data analysis method that requires the development of themes and sub-themes taken from the researcher formulated Topic Guide and from themes emerging from the content of interviews. These themes are then arranged within a thematic framework or matrix, which is the defining characteristic of this form of qualitative data analysis. Codes (descriptive or conceptual labels) are synthesised and attached to the verbatim data and then ordered within the framework by theme.[147]

The framework method of qualitative data analysis has been used since the 1980s, originally in policy research, but is now a popular approach in the organisation and analysis of health related research data, particularly in those studies utilising mixed methods in addressing research questions in health, such as ours. [148]

The main benefit of using Framework analysis is that it offers qualitative researchers a convenient structure in which to systematically refine data and is of particular use in qualitative research which:

- Involves multiple researchers
- Involves researchers working in a multi-disciplinary field

- Involves members of the research team who do not have experience handling qualitative data
- Utilises large datasets
- Involves data taken from transcripts of semi-structured interviews[148]

The primary researcher who conducted all the interviews was supported by two more experienced qualitative researchers in the identification of themes for the framework but was subsequently independently responsible for coding, ordering and interpreting the data using the thematic Framework method. An inductive method of analysis was used in interpreting the data. This was done by comparing and contrasting transcript content, between and within individual interviews in order to identify, refine and summarise key themes. A Computer Assisted Qualitative Data Management Software (CAQDMS), QSR Nvivo 10 was used for data handling during analysis.

RESULTS

Participants and Setting

Twenty-five interviews were conducted in the period between December 2012 and November 2013 on a cross-section of those patients recruited to the Missed HIV study (See Chapter 4) and completing the study questionnaire. Table 1 provides a breakdown of the demographic characteristic of those chosen for and completing a semi-structured interview with the investigator. All interviews were undertaken in an empty room within the HIV clinic and lasted between 20minuets and 1 hour 15 minutes.

Although the final sample of participants completing the semi-structured interview was representative of those completing the questionnaires, there were some challenges in achieving this sample with some researcher and clinic related factors impacting on the recruitment of participants and on the content of the interviews. For example, there was difficulty in recruiting some people of Black African ethnicity, particularly those of East African origin. This may be due to the fact that the primary researcher conducting the interviews was of East African origin and this may have contributed to some patients' decision not to participate in the study. This unease in discussing sensitive matters regarding HIV infection with an individual of the same ethnic origin and the potentially the same community also became evident in those who did choose to undertake an interview. The researcher was asked by four participants where she was from and a further two about her religious beliefs and this have contributed

to some of the reluctance or refusal to answer questions, particularly those questions relating to more sensitive areas of the Topic Guide such as sexual risk behaviour.

Clinic factors such as how the patient felt about their doctor or CNS or about the particular consultation that they had come from also played an important role in the likelihood of patient recruitment and vitally, the content of the interviews. This was illustrated clearly on one occasion when I was briefed on a patient by his doctor before conducting his interview and was told that 'He's given [HIV] to his beautiful, young girlfriend. Such a shame, she's so young and pretty.' Having not sat in on the consultation, I was unaware whether the doctor's thoughts had been picked up by the patient but from the interview it became apparent that the patient felt defensive, not mentioning his partner, refusing to answer any questions relating to sexual risk behaviour and choosing to leave the interview before all the questions in the Topic Guide had been covered by the researcher. In some instances however, interviews with participants were particularly fruitful because of a good relationship with their CNS or doctor with one participant agreeing to be interviewed because 'The doctor said it would be a good thing to do if I had the time'. This view of the researcher as an extension of the patient's clinical experience was consistent, with complaints of consultation or service often being associated with a poor interview or refusal to participate and positive relationships with clinical staff resulting in lengthy interviews, allowing the researcher the opportunity to build rapport and elicit more information from the participant, which was particularly useful when touching on the more sensitive areas of the Topic Guide.

Participant	Age group	Ethnic group	Gender	Sexual Risk	Diagnosis stage
1	>=60	Black British/Caribbean	Male	Heterosexual	Early
2	50-54	White	Male	Heterosexual	Late
3	45-49	Middle-Eastern	Male	MSM	Early
4	50-54	Middle-Eastern	Female	Heterosexual	Late
5	35-39	Black African	Male	Heterosexual	Early
6	35-39	Black African	Female	Heterosexual	Late
7	50-54	White	Male	MSM	Early
8	20-24	Black British/Caribbean	Male	MSM	Early
9	55-59	Asian	Male	Heterosexual	Late
10	25-29	White	Male	MSM	Early
11	45-49	White	Male	MSM	Late
12	40-44	White	Male	Heterosexual	Late
13	45-49	White	Male	MSM	Early
14	40-44	White	Male	MSM	Early
15	40-44	White	Male	Heterosexual	Late
16	40-44	Black African	Male	Heterosexual	Late
17	20-24	Middle-Eastern	Male	MSM	Early
18	>=60	White	Male	MSM	Late
19	40-44	Black African	Female	Heterosexual	Early
20	25-29	White	Male	MSM	Early
21	35-39	Black British/Caribbean	Male	Heterosexual	Early
22	25-29	Asian	Male	MSM	Early
23	25-29	Black British/Caribbean	Male	MSM	Early
24	55-59	White	Male	MSM	Late
25	30-34	White	Male	Heterosexual	Early

Table 1: Demographic characteristics of participants completing the semi-structured interview

Sickness, Health and HIV testing

HIV testing prompted by ill health was seen in several participants and in those patients experiencing extensive periods of ill health this was often very much dependent on the clinician taking the decision to test as there was a theme of a high level of deference to the health care provider in those having been severely ill in the run up to their HIV diagnosis. In some cases however there were indications of a health care provider's reluctance to test for HIV in these patients. Even when HIV was strongly suspected, this was not directly told to the patient and testing was not immediately requested. One interviewee recalls contact with a nurse at his GP surgery where he was told to go to the SH clinic after a diagnosis of oral candidasis with another interviewee experiencing extensive investigations under a respiratory medicine team being told he would be referred to another speciality for 'further testing'. It is clear that patients felt HIV was suspected by the health care providers at these times and that they had made the choice to refer the patient and not to test for HIV themselves. This left one interviewee feeling confused and embarrassed.

"When I was there she said she doesn't have the knowledge to diagnose what I had – not even on a non-professional limit. She didn't want to tell me… She said there's a clinic over here. I didn't know what type of clinic, mind. It might have been even described as a sexual health clinic. It wasn't a place where I really wanted to go, to be truthful with you… I've come to the clinic myself because it seems I've got nowhere else to go."

Participant 12 (Heterosexual man, 40-44 years)

These ideas were expressed by those patients who were aware and also conscientious enough to respond to the hints dropped by their health care providers and subsequently made the choice to test independently.

Some patients experienced long periods of ill health before being tested for HIV and were often resentful of the extensive investigation before a test was offered to them. The feeling that they relied on their clinicians to be able to identify the cause of their ill health coupled with frustration and disappointment at the lack of a definitive diagnosis was common in this group.

"I think I felt, in a way, I was just getting passed from pillar to post… It just seemed like they weren't listening. Obviously, if they would have listened to me properly, they could have found out that I had HIV

before because they would have tested… One of the doctors I spoke to said because of the nature of what I was coming in and complaining about, not many doctors would have checked to see if I had it. Obviously, somebody did, because that's how they found out"

Participant 16 (Heterosexual man, 35-39 years old)

Many patients however indicated that they had often been unclear to clinicians about their risks or possible exposures, even those suspecting possible HIV infection themselves did not always choose to discuss HIV testing with the clinicians and instead chose to hint at the idea of possible HIV exposure, disclosing risks such as sex with sex workers in Asia, travel in west Africa or a history of drug use, apparently in the hope that it might prompt HI V testing and there was a feeling of annoyance in some that this did not, on reflection, achieve this outcome.

"You know, I told the nurse that I worked all through West Africa. Now, single male working in West Africa – expatriate, they've normally got a lot of money. They're possibly at high risk of mixing, and having fun. That should be enough… to say in the clinic 'would you like a test?'"

Participant 12 (Heterosexual man, 40-44 years old)

The reasons for this non-disclosure are variable with some relating to fear of stigma, which is touched on later in more detail. However, some causes seemed to be due to cultural expectation with some participants expressing anxiety in disclosing sex out of marriage or homosexual intercourse due to their religion or cultural background and this seemed to come from a fear of being judged by clinicians. In others however, this lack of disclosure was due to a mistrust of the health providers or lack of faith in their ability to maintain confidentiality or simply the idea that some record of HIV testing would be kept and that this would mean they would be perceived poorly and therefore treated differently in future by health care providers who subsequently viewed their records.

Different obstacles to seeking health care were commonly expressed amongst the group. The obstacles expressed included personal circumstances or work, either being prohibited or discouraged by employers to take the time from work to visit a doctor or feeling that their work load would not allow for them to take the time required to visit their doctor.

"I was so busy. I was working from Monday to Sunday. 10 am to 7 pm I should be in even if I was getting a chance to go to the GP. After I left that post, because she was not even nice, treat like slave… it was so tight, so busy. Even when you're sick, like maybe headache or something, you just take paracetamol and continue. No time to even go. Even you can't think who is going to give you permission."

Participant 6 (Heterosexual woman, 35-39 years old)

More commonly however, system based difficulties in accessing the GP was expressed as a barrier to seeking health care. Several participants described that not only the process of securing an appointment with their doctor at a convenient time for them as difficult but also the long waiting period to see their doctor and the brevity of the consultation as a combination of factors that when taken together acted as a major obstacle to visiting their doctor, particularly if the ill health was minor or manageable.

"I think it's really hard having to ring up at 7:55 when you probably don't get through until 8:20 and everything else is booked up. It's just stupid… The service is so poor and I don't like it. I actually hate going to my GP."

"I don't understand GPs, I know they are busy but you can't give someone five minutes and think it is going to be okay. I have questions to ask. He said I will be fine and to go and see the chemist."

Participant 20 (gay man, 25-29 years old)

This difficulty in accessing the GP may have contributed to delays in diagnosis but was not in itself cited as a barrier to accessing HIV testing. Seeking an HIV test in other ways (e.g. through the Sexual Health clinic) did not have these barriers associated with it and many participants expressed a number of other issues in in accessing HIV testing through other routes and these will be explored later in the results.

Some participants, mostly those who did not experience long periods of ill health had a different view of their health and took HIV testing, either alone or as part of a sexual health screen, to be a normal, even an essential part of their health routine. This idea was more commonly expressed by gay men as a facet of overall good health, an important part of well-being and also a responsibility that one has to those they have sexual contact with. This particular theme is identified again and explored further in Chapter 6 among gay men who are regular sexual health clinic attendees. This is not a theme exclusively expressed by gay men however with health conscious heterosexuals in the sample also expressing this idea of

regular testing as an element of good health and a sign of responsibility, as illustrated in the respondent quoted below.

" I never thought that was going to be an issue, and, you know, quite frankly I thought it was just a responsible thing to do, to get tested, and that's kind of what I've been doing… when you come in, you just say, 'let's just do the whole shebang', then they'll do everything in one go."

Participant 25 (Heterosexual man, 30-34 years old)

Risk taking and HIV testing

Some participants aren't tested for HIV due to ill health and also did not necessarily work HIV testing into their normal health routine but chose instead to test for HIV on the basis of risk exposures, these were usually young, gay men who felt that they were able to accurately identify when they had experienced an exposure to HIV and self-initiate testing. However, among participants it was found that an individual's assessment of self-risk and therefore their requirement for HIV testing do not necessarily always correlate with their actual risk of HIV transmission. The reasons for this appear to be complex but several participants offered different explanations as to why this lack of congruence in perception of self-risk and real risk of HIV transmission exists. In some participants this appears to be due a temporal assessment, associating high risk sexual behaviour with a period when they were younger and strongly maintaining that they practice safe sex at present and therefore have not considered themselves to be 'high risk' despite many indicating that they had not had a test since the historic period of risky sexual behaviour in their youth.

"When I was younger, I probably took stupid, more risks... Now, I feel like because when I was in my thirties I was a lot more careful, and to think now, at my age, that I would have been more careful and that I was at low risk. Because, I didn't' do the stupid things I did when I was younger. So it was kind of a little bit of a shock now.

In a way, in my head, I sometimes thought, if I was going to get HIV, I should have done it when I was younger, when I've been stupid, not older when I thought I was more sensible.'"

Participant 24 (gay man, 55-59 years old)

Another theme that emerges among some risk based testers is that of different levels of perceived self-risk and the experiences that inform these. Some participants express weighing up how risky the type of sex they engage in is for the transmission of HIV, grading different sex acts as more or less risky based on their knowledge of HIV exposure and transmission. This becomes a particular problem when these grades of perceived self-risk are informed by a participant's previous experiences; when what is understood to be risky, is not followed by a negative consequence and reduces the level of risk previously associated with that sexual act in future.

"You know, there's high-risk and there's medium-risk and there's 'less-than-medium-risk', but, you know, just because you're in a lesser than high risk, that doesn't mean there's zero risk, and that's obviously proven by me being here today."

Participant 23 (gay man, 25-29 years old)

"About penetration and, most probably, that was the way in which I was infected. But I've never allowed anyone to come into myself, thinking that the main risk will be that; not only being penetrated."

Participant 10 (gay man, 25-29 years old)

"So after so many casual sexual partners, the question just gets thrown away. So the question of a health risk is hiding itself. So that becomes embedded within people's minds and they don't ask, and they don't necessarily think about it."

Participant 8 (gay man, 20-24 years old)

Several participants among this group also expressed the idea of sexuality being important in the risk of HIV exposure and this went beyond the higher prevalence of HIV among gay men but related to an expectation that if you are a gay man you will engage in high risk sexual behaviour, with a greater number of casual sexual partners. One participant describes being unable to identify with examples of sexual relationships in his largely heterosexual community as a young adult and recalls the feeling of being introduced to sex in the gay community which he felt was distinguished from heterosexual sex by being more high risk whilst another participant describes the sex culture of London's gay community as inherently risky.

"I think the reason why I necessarily didn't think about the risks too much is because within London's gay community, a lot of people tend to not question their sex. Promiscuous sex in London's gay community is a pandemic in my opinion."

Participant 8 (gay man, 20-24 years old)

Fear of Stigma and HIV testing

Fear of HIV testing or test result was not a very strong theme in the interviews and this might be because past feelings of fear are difficult to recall and express after being offered comprehensive advice and a having a better understanding of HIV and a past ignorance of the realities of living with HIV were commonly expressed by several participants. Fear of stigma however was commonly expressed by participants. This stigma manifested itself in different ways between participants but remained a strong theme among all participants. Some participants perceived stigma from clinicians, most clearly seen in the examples of those health care providers suspecting HIV infection, voicing a concern about this or indicating their suspicions but then choosing to refer the patient, leaving patients with the perception that HIV is not a condition some clinicians want to deal with or test for. However the majority of stigma relating to HIV testing was manifest in some participant's preconception of groups affected by HIV with a recurring theme of not identifying oneself with one of these groups and therefore not being at risk.

"No. It didn't enter my mind, I never thought of it at all because I'm clean. I've only ever been with one man. Also, I never had any other symptoms. No discharge or strange smell or anything like that. I was clean… I married when I was 16 years old and I've never had any problem."

Participant 4 (heterosexual woman, 50-54)

"HIV is labelled as a seriously homosexual… in many factors and many places, and the sexual clinic… there's a lot of working people [sex workers] here, you know - coming here. So it's hard for normal people to come and mix in that, you know, walk of life, just because they went out and got gonorrhoea or, you know, something."

Participant 12 (heterosexual man, 40-44 years old)

One of the most important areas where stigma impacts on HIV testing is in people's attitude to sexual health and the sometimes overwhelming reluctance and anxiety expressed by some participants in

attending the sexual health clinic to take an HIV test. Some participants expressed the feeling that it is a place they wanted to distance themselves from as much as possible due to the ideas that they had about other attendees, issues of confidentiality, and feelings of shame in attending the sexual health clinic. One participant expresses his severe reluctance to attend the sexual health clinic, he describes serious ill health and the need for surgery but after experiencing genitourinary symptoms in the period running up to the procedure he describes how he was *'forced to go in the end'* in order to avoid the embarrassment of what the surgeons might find.

"There's a high percentage of homosexual people, which some people don't like to be around. There's a high percentage of working people [sex workers] there. There's your drug addict, crazy people in there. It's a place which is not normal. It is not an easy place to be, I think…. It gives me the creeps, actually… It's a disorganised place, for high-risk people; but what happens if you're not high-risk? Once you're tested positive – you join the same club as them – but when you walk through the door, you want the same treatment as you walk into, like, a GP."

Participant 12 (heterosexual man, 40-44 years old)

This particular participant discusses his history of visiting sex workers both abroad and in the local area, which he cites as a deterrent to visiting the sexual health clinics. Despite these risks and also describing a history of being diagnosed with sexually transmitted infections, he had never chosen to identify himself as '*at risk'* and this appears to be due to a strong fear of being stigmatised or a self-stigma which he reflects onto others, such as those who attend the sexual health clinic. This participant however also stated an overall anxiety or fear accessing health care and has historically avoided any contact with health services, choosing to self-prescribe where possible and so, it is likely that much of this aversion to attending the sexual health clinic might be due to a general aversion to visiting health care services. However other participants, even other heterosexual men who do not describe any anxiety in accessing other health care services have described feelings of stigma which deterred them from attending the sexual health clinic.

"Because obviously, it was a stigma back then to come to the [sexual health clinic]. Obviously, people would know you were going because you've probably got… but they don't 100% know. Back then, it was just a

thing, if you're going to the [sexual health clinic], you've got something wrong with you. So people didn't really come here as much as they should have, if that makes sense."

Participant 16 (Heterosexual man, 35-39 years old)

This same participant goes on to describe how he was only confident enough to be able to attend the sexual health clinic when he went as a part of a group of other male friends, making a sexual health screen more acceptable or socially appropriate. However, even on these occasions, HIV testing itself was not acceptable to this participant.

"So, it was only a thing where we'd come every couple of months, we'd all go together, like a boys' thing… not for an AIDS test, an HIV test; just a health check."

Participant 16 (Heterosexual man, 35-39 years old)

Stigma surrounding sexual health generally but particularly HIV testing is a consistent theme and appears to be a real barrier for patients and some patients perceived this to be a real barrier for health providers also. Due to this stigma, many participants felt that HIV testing might be inappropriate out of specialist settings such as the sexual health setting however the sexual health setting is in itself highly stigmatised according the view of other participants.

DISCUSSION

Findings from the Missed HIV study indicate that patients seem to access HIV testing and come to be diagnosed through very different routes but that testing appears to broadly be prompted by one of three conditions; ill health, a perceived self- risk, or as a part of sexual health routine. Although these different routes appear to be associated with different population groups or demographic characteristics, such as gay men choosing to make testing for HIV a part of their health routine, there are many common themes shared by participants coming to be diagnosed through different routes, such as frustration in accessing their GP and a lack of satisfaction with their clinical consultation. Findings from both the questionnaire and interviews indicate that ever testing for HIV and regular testing for HIV are both associated with being White and MSM, which may go to explain why White MSM are consistently diagnosed earlier (with high CD4 cell counts) than black heterosexuals and this pattern is seen in our studies in West London just as it has been identified throughout the UK.[68,149, 150] The findings from this study however also go some

way in exploring why these associations are seen and how these different routes to diagnosis may impact on the timing of a patient's HIV diagnosis.

Risk-based HIV testing

The perception of a current low risk for HIV infection as compared to a period in the past was identified commonly in older gay men. This idea that they were once at risk but are not any longer due to relatively safe sex may be due to the realities of being diagnosed with HIV in the past, before the availability of effective ART, acting as a deterrent to testing for HIV. This is also likely to mean that these patients did not test for HIV following risky sexual behaviour when they were younger and have subsequently and incorrectly gone on to categorise themselves as 'low risk' individuals and delayed HIV testing. This lack of HIV testing in older patients is also seen in questionnaire findings which illustrate that patients 50 years of age and older are significantly more likely than those who are younger to have never been tested for HIV. Although this could be mostly due to a lack of awareness of HIV testing in older patients, this did not emerge as a strong theme form the interviews whereas surprise at current HIV diagnosis despite perceived current low-risk was common among several participants indicating that it may contribute to why older patients do not test for HIV regularly and why they are less likely to have ever tested for HIV.

A particularly interesting finding in those who describe risk-based testing practices is that of a lack of congruence in self-perceived risk of HIV infection and real risk described. This lack of congruence is not only described by participants but also supported by questionnaire findings, which show no correlation between recent (previous 12 months) risky sexual behaviour and having an HIV test in that time period. These findings have been seen elsewhere and the implications of this are important for the identification of recent HIV infection. In a UK study undertaken amongst MSM who present late in Brighton,[151] self-perceived risk of HIV acquisition was low and participants reported feeling surprised at their diagnosis, much like participants in our sample, MSM interviewed distanced themselves from 'high-risk' behaviours despite describing engaging in unprotected anal sex when asked directly. In interview analysis of 64 men and women for the Polaris HIV Seroconversion study in Canada, authors found that repeat negative testing for HIV frequently resulted in confusion as to what constitutes a risk and might even lead to thoughts of immunity to HIV.[152] This is likely to be acting not only as a form of positive reinforcement, increasing the practice of a high-risk sexual behaviour and potentially increasing the risk of HIV transmission but the 'down-grading' of certain high-risk sexual behaviours or reduction in perceived-risk

will also result in decreased testing for HIV, particularly among those who are risk-based tester and makes this means of testing particularly ineffective for the earlier identification of HIV.

Routine testing and Stigma in the Sexual Health Clinic

Testing for HIV as part of a health routine was a type of HIV testing commonly expressed by some participants, particularly young gay men. This was seen as an aspect of good health and also as a responsibility of an individual to their future sexual contacts. Patients diagnosed through this route of HIV testing were no less shocked by their diagnosis but were generally identified at an earlier stage. This practice of routine testing for HIV and its association with earlier HIV diagnosis was also identified in the questionnaire, with the median time from last negative test to positive diagnosis being 8 months (IQR: 3.5-24 months) in those testing regularly for HIV. These participants were however comfortable in attending the sexual health clinic and this is where they chose to undertake their regular sexual health screen and HIV test. Some participants however did not feel this way and expressed ideas that indicated a fear of stigma in attending the sexual health clinic. This was most commonly expressed by heterosexual men and described as a reluctance to attend a sexual health clinic due to feelings and ideas about a set type of person or groups of people at risk of HIV infection and a strong reluctance in some to identify themselves with these groups. However, as HIV testing continues to be seen as a large element of and exclusive to the sexual health clinic setting by some, it will continue to be inaccessible to those experiencing the greatest levels of denial and self-stigma which is manifested in reluctance to attend the sexual health clinic and receive an HIV test. Issues related to testing for HIV when initiated as part of a sexual health routine, such as the frequency of testing and the potential for other methods of regular testing are further explored in Chapter 6.

Ill Health and Provider initiated testing

Participants experiencing ill health, particularly those who had experienced extended periods of ill health for a year or more, commonly expressed feelings of frustration with clinicians and voiced feelings of resentment at having not been diagnosed with HIV earlier. Although it may be that a patient's view of what they expected of their health care providers is difficult to accurately assess in retrospect of their HIV diagnosis many participants suffering from ill health discuss poor provider practice, citing issues such as dismissiveness of symptoms in GPs and a lack of consistency in follow-up as a real issue even after the primary barrier of securing contact is achieved and there is a commonly expressed feeling that the

infection itself is of little consequence to those who present with ill health, as they only recall the severe ill health, investigation and ineffective treatments that didn't ameliorate their condition for long. This delay in identification of HIV positive patients was also found in the results from the questionnaire with only a third of patients questioned who presented with symptoms indicative of possible HIV infection, being diagnosed with HIV within a year. This picture of provider reluctance to appropriately initiate testing is further reinforced by the cases of clinicians suspecting HIV infection in their patient but choosing to hint at the possibility of infection or refer to another specialist in place of immediately testing the patient which not only increases the risk of the patient feeling stigmatised and anxious but also clearly goes to delay the identification of HIV infection in those who are already engaging with health care services.

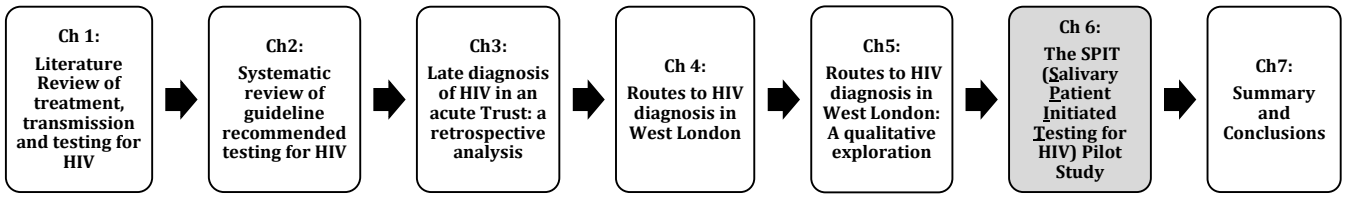
Limitations

Among the most important limitations of this study is the low level of participation of patients newly diagnosed with HIV within the ICHT. There was a particular issue in the recruitment of patients who did not speak English well enough to participate in either the questionnaire or the interview part of the study which may have led to the introduction of a systematic bias as it resulted in under sampling of some groups. Additionally, none of the women diagnosed with HIV during pregnancy consented to take part in the study despite being eligible and able to communicate. This is also likely to have contributed to an over sampling of MSM, which may have biased our sample and the topics identified. In addition to this, there were also some aspects relating to the researcher and the clinical setting, which have been described in Participants and Recruitment, that might have impacted on who was recruited and what was elicited from participants undertaking interviews. It is however reassuring that the sample of those completing the semi-structured interview with the researcher, were on the whole, representative of those recruited to complete the questionnaire, if not representative of all those eligible for participation. Additionally, although three researcher were involved in identifying the themes for the framework analysis of the interviews undertaken, only the primary researcher was involved in the coding, ordering and interpreting of the data for analysis and summarisation of findings which may have resulted in some underlying themes in the data being excluded or a lack of clarity in the characterisation of the significance of the themes identified.

CONCLUSION

The themes and summaries generated from qualitative analysis of interviews with HIV patients has provided possible explanations for the patterns seen in patient routes to HIV diagnosis and HIV testing practices. Risk-based testing practices expressed by some participants are likely to be ineffective in diagnosing HIV at an earlier stage due to lack of congruence in self-risk perception and actual sexual risk behaviour. Although regular testing for HIV as part of a routine is associated with more frequent testing it requires regular attendance to the sexual health clinic, which is not acceptable to some participants who fear the stigma associated with this setting. This stigma has been experienced by some patients from health care providers and is likely to be associated with the delays experienced by patients in being offered an HIV test.

Chapter 6: The SPIT (Salivary Patient Initiated Testing for HIV) Pilot Study



The findings from the Missed HIV study highlight important patterns in patient routes to diagnosis and attitudes to testing for HIV and go some way to explain the trends in HIV testing and diagnosis seen both within our local London Trust and nationally. Despite the inequity of access and diagnosis with HIV seen in different groups, particularly the increased risk of late stage of diagnosis in Black African heterosexuals compared to White MSM, the highest incidence rates of HIV transmission in the UK continue to be amongst MSM. In the following chapter, I will explore how inadequate testing may be contributing to transmission within this risk group and how a pilot of a model of testing outside the clinical setting may improve testing patterns within this at risk group.

INTRODUCTION

Men who have sex with men (MSM) remain the group most affected by HIV in the UK, with an estimated 41,100 (95% CI: 37,300– 46,000) men in this risk category living with HIV.[68] These figures are taken from PHE report on HIV in the UK and include incident cases, HIV prevalence and additionally HIV from unlinked anonymous sero-surveillance. Unlinked anonymous sero-surveillance provides an estimate of undiagnosed cases of HIV through GUM clinic survey data (from 13 sentinel GUM clinics) of gay men, where residual samples taken for routine syphilis serology is subsequently unlinked from any patient identifiers and tested for HIV. This method of unlinked anonymous serosurveys began in 1990 to accurately and routinely monitor HIV prevalence within defined populations such as MSM, not relying on gay men seeking a named HIV test and therefore reducing participation bias, this method increases accuracy in predictions of the epidemic amongst the group of individuals attending GUM services.[153] The potential bias this method introduces however is that individuals attending a GUM service being tested

for Syphilis are not necessarily representative of all MSM, but do represent high risk groups. Additionally, previous HIV diagnosis is also recorded from samples to eliminate those already known to be HIV positive from the undiagnosed estimate. The number of undiagnosed MSM living with HIV, estimated from this survey is 7,300 (95% CI: 3,700–12,300), which accounts for 17.8% of total HIV infection amongst MSM.[68]

Incident HIV infection in MSM has represented the largest number of new infections in the UK since 2011 with an average 2,400 (1,600-4,100), accounting for over half of total new diagnoses annually and this has been increasing with the highest number of new HIV diagnoses amongst MSM being reported in 2012 with 3,250 new diagnoses.[1] In a study of HIV incidence in MSM undertaken by PHE data from 2001-2010, it was found that this increase in incidence was not only due to an increase in diagnosing the undiagnosed fraction although the uptake of HIV testing amongst MSM had increased 3-7 fold, with a reduction in estimated MTD (mean-time–to-diagnosis) from 4.0 years in 2001 to 3.2 years in 2010, as neither HIV incidence or total undiagnosed HIV infection changed significantly during this decade, indicating an overall increase of new infections has accompanied the increase in HIV testing.[154]

High HIV testing rates continue to be seen in MSM attending sexual health (SH) clinics; 84% compared to 76% seen in heterosexuals attending the same settings in 2012.[68] However, as described previously (Chapter 2), HIV testing in these settings is insufficient for attaining significant reductions in undiagnosed HIV infections, and nowhere is this more evident than amongst MSM, where high HIV testing rates, largely in SH settings, has not had the impact required for the earlier identification of HIV positive MSM, which could also eventually lead to the earlier treatment and reduced sexual risk required for the reduction of onwards transmission. In order to increase broader HIV testing rates , HIV testing must move not only beyond the SH/GUM clinic to wider clinical settings but also beyond the clinical setting to the community with novel models of delivery that make testing, particularly repeat testing in high-risk groups such as young MSM, as easily accessible as possible.

Without knowing the HIV status of patients, it is impossible to implement any risk reduction strategy appropriately and only with repeated testing, ideally offered after every HIV exposure can an intervention significantly impact on population level HIV incidence as well as late presentation. Therefore our project aimed to encourage repeat HIV testing amongst high risk individuals who may be engaging in high-risk sexual behaviour based on the results of a previous HIV test, without an awareness of current serostatus.

Self-sampling pilots amongst MSM

During the study period self-testing for HIV was not legal in the UK. Hence self-sampling only was a feasible option to encourage repeat HIV testing. As a means of increasing HIV testing in a wider range of settings PHE launched several pilot programmes funded by the DH, which assessed the feasibility, acceptability, effectiveness, cost-effectiveness and sustainability of a range of HIV testing projects. Pilot AB8, was a self-sampling and home testing pilot for MSM in Sheffield and offered saliva home-sampling kits to MSM over a 4 month period from June to September 2009. 126 kits were distributed and there was a 47.6% return rate, with 75% of those returning samples <30 years of age and had >1 sexual partner in the preceding month. However, there was no new diagnosis of HIV infection in this small pilot.[155] A seropositivity rate of 1.4% was identified in a postal self-sampling project for HIV testing, which was piloted by the Terrance Higgins Trust (THT) and PHE over a 3 month period from January-March 2012. In this much larger pilot, 3,235 self-sampling kits were distributed and there was a higher return rate of 61%. Kits were made available via the THT website and were advertised to gay men in the gay press and dating sites without the necessity for initial SH clinic attendance to obtain a sampling kit.[156] these pilot studies show that amongst high risk groups for repeat self-sampling for HIV is acceptable. Although the THT pilot had a procedure in place for positive tests, only 13 of the 28 men testing positive for HIV were successfully linked into HIV specialist care in their local area with two of the men declining all further contact. This highlights the continued importance of effective linkage into specialist care services and the challenges that may be encountered to this when direct contact with health services is taken out of the HIV testing process and this is one of the primary concerns associated with this method of HIV testing.

Despite difficulties for linkage into care in some cases, self-sampling as a means of testing for STI such as Chlamydia and gonorrhoea has been shown to be both feasible and acceptable for MSM. In a self-sampling STI pilot undertaken in Brighton 334 eligible MSM were invited to self-sample for chlamydia and gonorrhoea using oropharyngeal and rectal swabs with 274 returning swabs and completing a questionnaire. 96% found oral self-sampling to be a feasible method of testing for these STI and the majority of participants also expressed a willingness to use this method for testing in future.[157]

The SPIT Study – Hypothesis, aims and objectives

Based on the evidence in support of different models for expanded testing for HIV and the evidence seen from various self-sampling studies amongst MSM, the availability of home-based salivary self-sampling

for HIV testing will be found to be both feasible and acceptable to young, high-risk HIV negative MSM attending our West London gay men's sexual health clinic and that there will be an increase in repeat testing rates for HIV in this group.

Aim:

- Assess the frequency of HIV testing amongst individuals who self-sample compared with their reported testing behaviour in the preceding 12 month period;
- Assess the feasibility and acceptability of self-sampling to this population.

Objectives:

- Measure the frequency of HIV testing 12 months before and 12 months after the use of home-based saliva testing through swab sample collection;
- Compare reported sexual behaviour and STI rates in the period before and after the availability of home-based saliva self-sampling through questionnaires;
- Assess the acceptability of repeat HIV testing with home-based oral swab collection through semi-structured qualitative interviews.

METHOD

Study Design

This study was a 12 month observational mixed methods study, comparing levels of HIV testing before and after the availability of home self-sampling swabs.

The study was funded by the British HIV association (BHIVA) research awards. A protocol was developed, submitted to and approved by local ethics committee (12/LO/0556).

Materials, Sample Collection and Procedure

Oracol+, a saliva collection kit designed by Malvern Medical Developments was the devices chosen for use as the self-sample swab for the SPIT study. In a comparison of oral fluid collection devices (including OraSure, Omni-SAL and Oracol) sampling for Enzyme-Linked Immunosorbent Assay (ELISA) testing for rubella specific antibodies, Oracol sampling devices were found to provide oral fluid samples with the

higher relative mean titres of total specific antibody than other saliva self-sampling swabs and were also found to be highly acceptable to participants in a previous study comparing oral fluid self-sampling devices.[9] This oral fluid collection device is additionally the preferred means of sample collection by the St Mary's hospital laboratories for ELISA testing for HIV-1 specific antibodies, where the study was undertaken.

Participants recruited to the study were asked to follow a specific procedure for sample collection, soaking the pink tip sponge below their tongue and rubbing it across the inside cheek for a minimum of 30 seconds to allow for maximum saliva absorption for sample collection. The swab was then placed, sponge first, into the microtube at the base of the device before the serrated end is broken and the top of the tube is sealed tightly to prevent leakage or aerosol contamination.

All samples were addressed to a PO BOX local to the St Mary's hospital, which was checked weekly for samples by the study researcher. Samples were processed and sent to laboratories along with all other patient samples requiring pathology testing collected for the day in the sexual health clinic in the Jefferiss wing at St Mary's hospital. A member of the nursing team checked for results from the laboratories once a week and these were immediately sent out to participants via the NHS communication systems via the participants' preferred means of contact, once received. The predicted turnaround time given for this process (from collection to receipt of result) was 10 working days or two weeks. The procedure for indeterminate or positive result was outlined in the study protocol (see Appendix R: SPIT Study Protocol) and involved a message inviting the participant to arrange to attend the sexual health clinic as soon as possible and a note being attached to the participant's SH appointment record indicating they were enrolled in the SPIT study and that a confirmatory HIV test would be required. A participant reminder was sent out via text message to all those recruited to the study to remind them that saliva samples were still being collected for HIV testing in January 2013.

Setting and Recruitment

The Jefferiss Wing at St Mary's Hospital is a large central London teaching clinic with over 50,000 GUM visits annually. The on-site HIV clinic has over 2,800 regular attendees (those attending the clinic more than once). Between ten and twenty new HIV diagnoses are made per month, mostly through the GUM clinic

but also in hospital inpatients across trust with the majority of new infections being amongst the younger MSM attending these clinics.

The GUYS clinic at St Mary's hospital is a dedicated service for young gay men. It sees men aged up to 35 years old for comprehensive sexual health screening including STI and HIV testing and treatment, safe sex advice and condom distribution. There are on average 800 attendances per year to this early evening clinic, which offers appointments or walk-in service between 6 pm and 8 pm on one evening each week.

50 men were recruited to the SPIT study from the GUYS clinic between May and December 2012. Men attending the GUYS clinic were invited to participate if they were over 18 years of age, able to give written informed consent, had a sexual health screen including a point-of-care test (POCT) with a negative result, and would be resident in the UK for the duration of the study follow-up period (12 months). Men were excluded from enrolment if they were known to be HIV positive, had a reactive POCT during their sexual health screen or suggested symptoms indicative of seroconversion. Individuals were also excluded if they were not felt by clinical practitioners to be appropriate for enrolment based on mental health issues, capacity or any reason that might hinder ability to give informed consent (see Appendix P: Patient information sheet (including eligibility criteria and consent form). Eligible HIV negative MSM were offered to enrol into the study and if agreeing to this they were reviewed by the research team where the study was explained to them. Individuals were then invited to enrol into the study and the informed consent sheet was explained to the potential participant and signature obtained in accordance with Good Clinical Practice (GCP).

An initial sexual behaviour 'baseline questionnaire' was completed by each consenting study participant and included basic demographic information; data on recent and previous HIV testing, sexually transmitted infection acquisition history and recent sexual behaviour. This information was self-completed by participants by the means of pen and paper questionnaire without the study researcher present in order to reduce the risk of reporting bias (see Appendix Q: Template of Baseline and End-of-study Questionnaire). Subsequent to questionnaire completion, each participant was shown how to use the swab to collect a saliva sample, this was explained and a sample was taken at baseline. It was also explained to participants that despite the method of testing used on saliva samples having a good sensitivity of 96.2%-100%, if correctly sampled.[160, 161] This positive identification rate is seen in the period subsequent to the first three

months following infection, known as the 'window period' and if there was concern over a recent potential exposure that they should use the emergency walk-in facilities of their nearest sexual health clinic. A formal sexual health education process was once again explained to all participants with provision of condoms and safe sex, and risk reduction strategies were discussed with the clinical and research teams. Participants were also advised that swab self-sampling should not be used as a replacement for a regular sexual health check and they should continue these as is normal to them. The option of collecting more swabs from GUYS if required was available and the contact details of study researchers were given to each participant in case of any further queries regarding the study procedure.

Each participant was then given six stamped addressed envelopes, each containing one Oracol+ swab, with a diagram reminder for its use and a contact form to indicate preferred method of contact for the result. Study participants could attend the GUM walk in service at any time throughout the study period

Recall

All participants recruited to SPIT were invited back to GUYS clinic at 12 months following their recruitment to complete an end-of-study sexual health screen, questionnaire. Information collected in the end-of-study questionnaire included STI history, sexual risk behaviour and HIV testing in the preceding year (see Appendix Q: End-of-study Questionnaire Template). Additionally, at this point 5-10 participants would be invited to complete a semi-structured interview with a researcher lasting approximately 30 minutes to assess the acceptability of saliva swab sampling as a means of testing for HIV infection (see Appendix S: SPIT Study Topic guide). These patients were recruited using a convenience sampling method as due to time constraints for many participants a judgement or purposeful sample based on demographic classification could not be undertaken. Where participants did not return for a recall session at 12 months from recruitment, they were offered a phone interview or email questionnaire to complete the End-of-study Questionnaire. Those participants who were unable to attend for an end-of-study sexual health screen or complete the questionnaire had their basic data on STI diagnosis, HIV testing and sexual behaviour extracted from notes on their last clinical attendance as per protocol.

Data Analysis

The primary outcome was the difference in the total number of HIV tests reported for the 12 month period before enrolment into the study and the total number of HIV tests (either through oral swab sampling or

clinic attendance) reported for the 12 month study period. Secondary outcome measures included difference in the total number of STI diagnoses in the 12 month period before and after recruitment to the study along with difference in the reported number of sexual partners in the three months before and study recruitment and the three months before study recall. Additionally at baseline, characteristics of SPIT participants were compared with a recent audit of the GUYS clinic to assess bias in recruitment by age, sexual behaviour and previous STI and HIV testing A chi-square (χ^2) test for significance for between-group differences was undertaken to assess difference in these measures and results were considered significant if $p<0.05$.

A regression model was used to assess associations between risk indicators (i.e. number of sexual partners and STI diagnoses) with number of HIV tests in the study period. As well as assessment of correlation between demographic factors such as age and attitude to swab self-sampling at baseline with number of HIV tests taken in the study period. Crude and adjusted odds ratios were calculated for each model, along with Clopper-Pearson 95% confidence intervals. Data input was compared in Microsoft Excel 2010 along with data cleaning and primary coding. Further data cleaning, coding and all quantitative data analysis was undertaken in Stata 12.0 (see Appendix T: Complete Stata Code SPIT Study).

All interviews for the qualitative aspect of the study were digitally recorded and transcribed verbatim. The semi-structured interview transcripts were then imported into Nvivo 10 (QRS International Pty Ltd) for coding and analysis using the framework method, which is described in Chapter 5. Themes were identified based on the topic guide areas and any themes which separately emerged and reoccurred independently in the transcripts were also included.

RESULTS

Refusal to join the SPIT study was not systematically recorded as only those interested in participation were referred to the research team for participation by the clinicians seeing patients in the GUYS clinic. It is therefore not possible to evaluate coverage of the study and reasons for declining participation. Following recruitment of all fifty participants, data from the baseline questionnaire, including demographic information, was compared to data taken from a previous audit of HIV testing, STI history and sexual behaviour undertaken on GUYS patient records in March 2011. This audit covered information on 256 patients who had attended GUYS in the 12 months from March 2010 to March 2011. Relevant

comparable variables included age at most recent attendance, median number of reported sexual partners in the last 12 months, number of STI diagnoses and number of HIV tests taken in the 12 month period prior to last clinical attendance.

We found no significant difference in age at last clinical attendance which was 26 years amongst the GUYS patients and 27 years in those recruited to SPIT (p=0.88). There was also no significant difference in either the reported median number of sexual partners, which was 2 in both groups (p=0.67) or the proportion being diagnosed with at least one STI in the 12 months preceding clinical attendance, which was 22.7% amongst those recruited to SPIT and 19.9% amongst those attending GUYS (p=0.77). The number of HIV tests taken in the last 12 months was also the same in those recruited to SPIT and GUYS wider clinic population and this was 1 test on average in both groups (p=0.67). As we saw no significant difference between these two groups here, we considered that those recruited to SPIT were comparable and representative of the wider GUYS population.

Outcomes

Forty-one of a total 50 participants had HIV testing, STI history and sexual behaviour data available at recall with nine patients lost to follow-up. These included 4 patients who did not respond to phone calls and emails or had provided incorrect contact details and five for whom a recall appointment was arranged but then subsequently did not attend (DNA). No HIV testing information was available for any of these participants. One patient received a positive HIV POCT result in the sexual health clinic 5 months into the SPIT study, and was unresponsive to recall attempts. Only 15 (30%) participants returned any swabs: 10 sent in one swab, 4 sent in a total of two swabs and 1 participant sent in four swab samples for HIV testing (i.e. a total of 22 swabs). The one patient who was diagnosed with HIV during the study period did not send any samples for the study in the 5 months of involvement in SPIT and before being diagnosed with HIV. Figure 2 illustrates these outcomes for all 50 participants recruited.

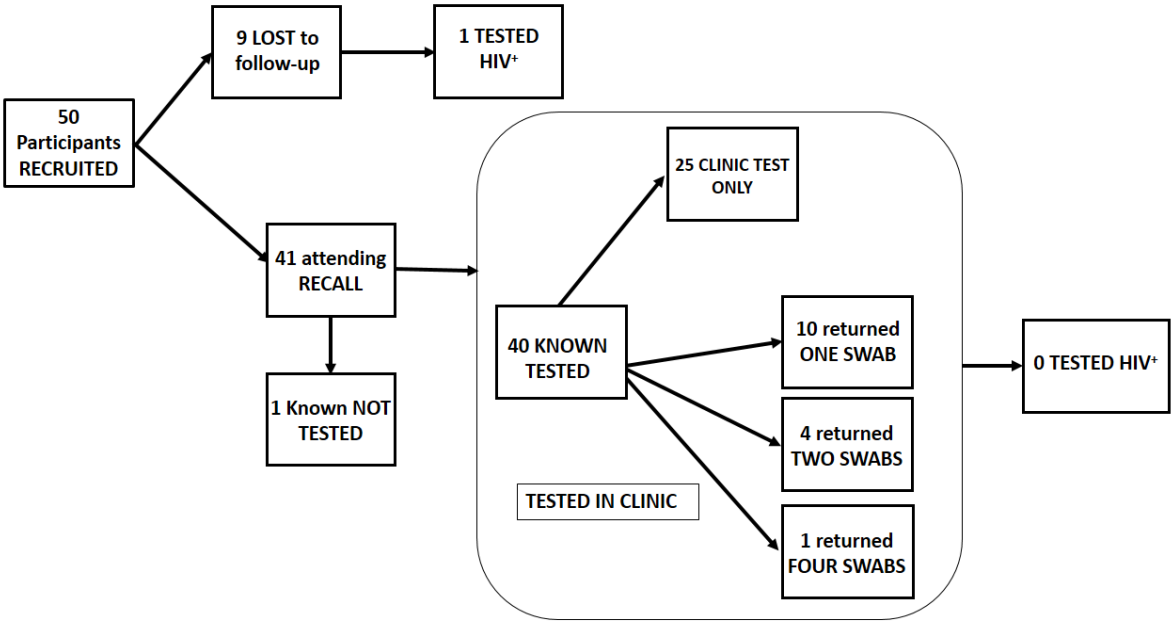


Figure 1: Flow diagram of testing and diagnosis outcomes of SPIT participants at end of study

Forty of the 41 participants with data at end-of-study had tested for HIV in some way (either through the saliva self-sampling method or through POCT in clinical attendance) over the course of the study period, with a median of 2 (IQR: 1-3) HIV tests in the 12 months period. This was significantly higher than the median number of HIV tests taken in this group in the 12 months before being recruited to SPIT, which was 1 (IQR: 1-2), p=0.04. When excluding testing from swab self-sampling, the difference between HIV testing levels in the year prior to study recruitment was not significantly different from the year after, p=0.43, suggesting that the increase seen in numbers of HIV tests may be due to the testing from swab self-sampling. All 15 participants who sent in a swab had come in to the clinic at least once in the 12 month period and also had another HIV test as part of their sexual health screen. The remaining 34 who had tested at all for HIV in that study year had come directly to the clinic at least once but had not sent in a swab sample. The one man recruited and attended a recall session who did not test at for HIV in the 12 month study period had reported 2 sexual partners in the 3 months prior to study recall but had reported that sex acts were protected and there was no record of STI diagnosis for this participant in the study period.

Amongst the 15 participants who had sent in a swab there was an average of 18 weeks between recruitment and the first swab sample being taken, this ranged from 5 weeks to almost the full year at 51 weeks. There did not appear to be any association with longer duration to first swab sample date and risk

of STI diagnosis during the study period. The average duration of time elapsing between the date of the first swab sample being taken and the date the second swab was 25 weeks and this ranged from 7 weeks to 32 weeks among the 5 participants who sent in a second swab sample.

Sexual risk behaviour

There were no significant changes in sexual risk behaviour with reported median number of sexual partners in the three months prior to recall and the three months prior to study recruitment being 1 and 2 respectively (p=0.24). Eleven of the 41 followed-up (26.8%) were diagnosed with at least one STI during the study period, this included one new case of chlamydia, 7 cases of gonorrhoea and four cases of syphilis. This proportion of STI diagnosis was also not significantly different from the period before study recruitment, which was 22.7% of 50 recruited (p=0.24) suggesting that there may have not been an increase in risky sexual behaviour within the group if STI rates are taken as a proxy for sexual risk behaviour.

Only 1 of the participants who sent in any swab samples was diagnosed with an STI in the year of the study. Interestingly however only 36.4% of those who were diagnosed with an STI during the study period tested more than once for HIV and the odds ratio of testing more than once during the year if diagnosed with an STI, compared to those not diagnosed with an STI was 0.25 (95% CI: 0.05-1.05) however this was borderline significant at the 5% level with p=0.058. There was also no association found between the reported number of sexual partners in the three months before study recall and repeat testing for HIV.

Swab use

Questions about sample use and procedure were answered by only 17 participants as this was the total number of study participants who actually sent in a swab during the study period (see Appendix Q: Section C: Practicalities of saliva testing). Six participants reported that they strongly agree or agree that it was easy to take a sample and a further five reported that they neither agree nor disagree that it was easy to take a sample. 16 thought that the instructions provided for taking a sample were clear. However, when asked if all results were received in the two week time period set almost half (46.2%) had said that they did not receive their result in this time period. Despite these responses, 16 strongly agreed or agreed that saliva home testing would make it easier for them to test for HIV in future.

Qualitative Findings

Six of 8 participants invited for interview at the end-of-study recall session took part in semi-structured qualitative interviews. Interviews lasted an average of 20 minutes and ranged from 13 to 40 minutes. Two participants had not used the self-sampling swab at home or sent in a sample and the remaining four had and all had tested at least once for HIV during the study period either through both swab use and rapid testing in clinic or solely through rapid testing in the clinic. Differences between those using different methods for testing and ideas and attitudes to testing using the home self-sampling swab were assessed. Findings from the thematic framework analysis are presented below, organised by themes emergent from analysis.

Saliva self-sampling swab as a method of testing for HIV

Many participants expressed ideas supporting use of the swab to test for HIV due to issues relating to clinical attendance including, long journey times and long waiting times for an appointment and feeling uncomfortable with clinical staff or the procedure for HIV testing (including an aversion to blood samples being taken and even the anxiety associated with the waiting period of rapid testing). However most participants stated that the benefits of clinical attendance, outweighed any of these drawbacks. Here participants were indicating that the issues with clinical attendance were things that others might find a particular obstacle but that these were obstacles which they were, on the whole, willing to overlook for the sake of getting the result of their HIV test immediately.

'Yeah, you have someone examining you and stuff, and that's not… not particularly nice … and then, you know, having the blood tests and everything - but the swab test is… it's more anonymous. You can just send it off - you know, you're not seeing people face-to-face. But in all honesty, I don't think that's ever been too much of a… an issue for me. I just, kind of, wanted to get the test done; that was all that… you can get the full test; there's no way of having that… that full test done, so I think that's important to do that every so often,'

(SPIT, participant 1)

'Yeah, I think… I think the swab is easier to do, for me, than the anxiety of that 15-minute wait… So that anxiety is really… really bad. But if [you're]… having a swab, and sending the swab away in an envelope, you can [still] worry - some people are worriers. I'm not. I mean, as preference, I'd have a blood test.'

(SPIT, participant 4)

There were also inherent issues with use of the swab itself including challenges in using the swab to self-sample and a lack of confidence in saliva samples compared to blood samples and delay in receiving test results, which put participants off using the swab more than once.

'The instructions - they weren't too bad, but it wasn't obvious. I had to, sort of, read and re-read them, and, kind of, double check, and thought, you know, 'does the… at what point do I snap off this bit, and does it go… which way round…? I don't know... It was a bit confusing.'

*(*SPIT, participant 1)

'Well, I just… it's not as invasive, in a sense of… it's in your bloodstream, and, you know… that's where people test it form; but, you know saliva… you know, I was chewing chewing gum earlier. Does that… does the chewing gum affect the result? So, you know… there is room for error, I think, on that.'

(SPIT, participant 4)

'Well, I used it once, and what happened was that I didn't get a result, and then I came here…And then after a while, like, after, I think, three weeks or so, I got the text to say that the result is negative.' The waiting time for results outweighed the hassle of having to attend in person

(SPIT, participant 5)

Interestingly, despite the difficulties of swab use being raised and the apparent preference for clinical attendance over home self-sampling, all participants were in support of the swab being made available for themselves and for wider use in future and this apparent approval in the use of the self-sampling swab to test for HIV was the same amongst those choosing to use it during the study period and those who did not use the swab to test for HIV. Several participants voiced this as a useful option for *'other people'*, those unlike themselves, who do not regularly, if ever attend the sexual health clinic. One participant talks about how the swab might be of use for someone like his heterosexual flatmate who is reluctant to get at sexual health screen, as it would allow him to test for HIV without having to attend the sexual health clinic. The sense is that the availability of swabs is most useful for those reluctant to attend the clinic or for the swabs to act as a potential back up option in case they were unable to attend the sexual health clinic as usual.

'Well, I think… I think it feels reassuring to have another method of testing that's available that's easy, that I can…you know, if I can't get round to actually getting into the clinic…'

(SPIT, participant 3)

'I think that the thing about HIV testing, and the reason why it's good to have so many options available, is because people approach their sexual health in really, really different … if you've got some closeted gay man, he's unlikely to come and get tested for… because, you know, he's… doesn't feel like that's him… And similarly, people who don't have a lot of sex, and don't identify it with their, kind of, sexual health as much, I think probably don't feel like going to a sexual health clinic is something that people who don't have a lot of sex need to do - because… it's almost, like, stigmatised, being something for who, like, have so much sex they need to be checked, you know. '

(SPIT, participant 6)

HIV and STI testing

As identified in Chapter 5, many of those testing for HIV did so as part of and established sexual health routine; wanting to test for a range of STI, in a clinical environment and with health professionals at hand and this way of testing was not only acceptable but also preferable to them as many recall testing for HIV in the past and express how the process has improved a great deal indicating that they had become accustomed to the improved methods of testing for HIV infection over the years.

'I mean, I get tested very regularly anyway, so I was like, kind of… just didn't do [the swabs] any more… HIV's not my biggest concern, in terms of sexually transmitted diseases I might get - it's more like chlamydia or gonorrhoea, stuff that could be passed orally. So I probably would have still come for screenings the same amount if I'd been using them.. I think the… sometimes the reassurance of someone, like, testing you for other things as well, and, like, knowing what they're talking about, and asking you questions, is really helpful.'

(SPIT, participant 2)

'It sounds like it would be very convenient and useful to me, but at the same time I wonder if I might still have to actually go in to access services at the clinic with about the same frequency, for other reasons - like for other tests, or for… And then I thought actually, I should probably come into the clinic for another set of tests

generally, and then I thought I… 'well,' you know, 'should I… is it worth me sending this off now anyway, if I'm going to…'

(SPIT, participant 3)

The routine attendance to the sexual health clinic meant that there was a lack of need or urgency associated with use of the swab and that it was considered as having no established place in testing practice and could simply be considered an additional option to be used in a number of other circumstances but few that participants could relate to themselves. Sexual health education has meant that for this experienced group of high risk MSM there is a close linkage between HIV testing and general sexual health check-ups which is why HIV testing alone is not sufficient incentive to make HIV testing preferentially taken up over all tests being done together with results available in real time for most.

'There wasn't any symptoms or any need, or any risk, or anything like that - just… it's just been, you know, just me and him…'
(SPIT, participant 6)

I've only used it once, in the last months… I haven't felt the need to use it before; I've… I kept meaning to do it, but I didn't do… I think there was no urgency to it, because I felt like I didn't need to test myself. I think that's probably it. And that I'd been in for a screening in February as well, and… that was actually to… because I was doing a Hep… I think the Hep B vaccinations…so that was the reason I came into the clinic, and I thought while I'm doing that, I'm… get the full check-up done as well. '
(SPIT, participant 1)

DISCUSSION

HIV testing in SPIT

Overall, 40 of the 41 (97.6%) participants followed-up had tested for HIV at least once during the study year and 62% of these tested more than once either by using the saliva self-sampling swabs and/or by attending the SH clinic and receiving at POCT or laboratory serum based test. An increase was seen in overall HIV testing frequency during the study period compared to the year before amongst this group of

young, high-risk MSM. This increased testing on average by 1 test per participant more than at baseline, pushing the testing levels of this high-risk group into the recommended testing level of more than one test per year. Although the majority of repeat HIV testing in this cohort was not through oral swab self-sampling it appears that being part of this study has encouraged more frequent HIV testing.

Despite this however, overall uptake of swab self-sampling amongst the group was only 30% of those recruited to study returning a swab to test for HIV. Compared to similar pilots such as the scheme piloted by the DH in Sheffield and the THT nationally, which saw swab sample return rates of 48% and 61% respectively, this swab return rate was low.[156] The higher return rates here may have partly been due to how self-sampling swabs were available to participants, with both the DH pilot having an online ordering element and the THT pilot being solely an online ordering scheme, where participants would order a single swab when they chose to as opposed to our method of systematically giving each participant a pack of swabs at baseline, which they could choose whether or not to use. The other key difference is the comparison of other care options. For our study participants the alternative to repeat oral swab HIV testing was attendance at a dedicated evening clinic that offered immediate real time HIV testing as well as full sexual health check-up. In contrast the other 2 studies, where HIV test kits were ordered through internet request, with a different standard of care options.

Despite the overall low return rate of the saliva self-sampling swabs, those participants that chose to use the swabs did space them regularly with the time between each sample being on average over 3 months, this also indicates that participants considered the window period of test sensitivity before sending in a sample.

Sexual risk behaviour and HIV/STI testing

There appeared to be no change in sexual risk behaviour and STI acquisition rates during the study period from the year prior to this indicating that swab availability did not impact on sexual risk behaviour. This was quite clearly echoed in the results of the qualitative analysis with all participants stating that this had not occurred in their case and they felt there was no reason to for them to change their sexual behaviour due to the availability of home self-sampling for HIV testing.

Further analysis of data looking at sexual risk behaviour in those not testing at the recommended level of >1 HIV test per year in this group showed that in this small study there was no association with

increased HIV testing and risk of STI diagnosis or average number of sexual partners in the 3 months before recall. The one participant who did not send in a swab but did acquire HIV during the course of the trial period was not only lost to follow-up to our study but also lost to clinical follow-up following his positive HIV POCT results. He could not be contacted for confirmatory testing and potential linkage to HIV specialist services. This meant we were unable to explore this participant's reasons for not testing previously using this method or getting a better understanding of their HIV testing behaviour and potential barriers to increased testing for them personally.

When looking at the testing practices of individuals in this group, the apparent lack of correlation between sexual risk behaviour and repeat HIV testing is also seen. Although participants did described how they related their sexual risk behaviour to their HIV testing practice, definitions and descriptions of risk was variable between participants, with those at comparatively low risk to others, viewing the same level of risk and choosing to test the same amount for HIV. This lack of congruence in self-risk perception and actual sexual risk behaviour was also identified amongst participants newly diagnosed with HIV in Chapter 5 and has been shown to impact on the level of HIV testing undertaken elsewhere in the UK and Africa.[163-166] In an American survey comparing self-perceived and reported sexual risk behaviour in a cohort of Emergency Department (ED) attendees, it was found that only 16.3% of participants who had no self-perceived risk for HIV also reported no HIV risk behaviour however, this was undertaken in 'non-high risk' ED attendees, excluding MSM and IDU attendees.[163] In another survey recent survey undertaken amongst MSM in South Africa, a majority 57% of participants also indicated that they had not undergone recent testing for HIV because they felt they were not at risk, despite an STI diagnosis in the last 24 months.[164] As discussed in Chapter 5 and in light of the current literature, self-perceived risk is likely to be acting as a form of positive reinforcement, increasing the practice of high-risk sexual behaviours and potentially increasing the risk of HIV transmission.

Saliva swab self-sampling for HIV testing

Reasons for the low return rate for saliva self-sampling swabs is variable and may be due to several factors, some of which have been identified in the results of the qualitative aspect of the study and partly relate to participants' perceptions of their sexual risk behaviour (as discussed above) and its relation to HIV testing. But additionally, the lack of a clear perceived role for the self-sampling swab in participants' HIV testing routine; due in part to its comparative weaknesses as a means of testing for this group of

regular sexual health clinic attendees. Firstly, the time taken to get results compared to immediacy of POCT did not outweigh the time needed to attend a clinic appointment for participants. Secondly, there was a correct concern by study participants that they should have a full STI screen not just an HIV test and finally there is some perceived distrust of the swab compared to routine clinic attendance, a method participants are more familiar with and hence feel is more robust. Clinical attendance was perceived as preferable due to issues such as those involved in receiving HIV result over real time POCT result and in particular, the emphasis placed on wanting to test for a variety of STI was highlighted amongst participants as a potential barrier to increased swab use and this has been echoed in other patient groups testing for HIV/STI using home sampling kits in Brighton.[157] In this study, participants were interviewed regarding their feelings on home testing for chlamydia and gonorrhoea, some felt it was 'silly' to test for only one type of infection when there was the option of testing for several through clinical attendance and many voiced a concern over their own knowledge in test administration and symptom awareness in initiating testing themselves, much like respondents in our sample.

Anxiety over aspects of testing specific to home self-sampling was also seen in this group, with issues over postal sampling and accuracy of results from samples that were patient administered being a cause for concern[20] this was quite clearly seen in some of those respondents in SPIT who expressed issues over accuracy and difficulties in self-sampling as a means of testing for HIV compared to clinical attendance. It is also possible that the delay experienced by some in receiving their results might have had an impact on whether some participants chose to repeat swab self-sampling. It is unclear however whether these delays were due to postage, sample collection time, laboratory analysis or results follow-up and delivery as this chain was managed by different nurses and researchers at different points.

A lack of need or urgency was stated by some respondents as a reason for not sending in a swab or not sending in more swabs. These participants had attended the SH clinic at least once during the study period and were, as a group, regular SH clinic attendees and having been recruited in an extended hours, dedicated gay men's SH clinic and all respondents felt that they were testing for HIV regularly enough to not feel the need to use the self-sampling swab for HIV testing more frequently. This perhaps illustrates a need for ongoing risk reduction education to counter low perceived self-risk and in order to continue to engage high-risk MSM in regular testing for HIV.

Despite the low rate of swab return all participants thought that the availability of an additional means of HIV testing was useful, either for themselves as something of a 'back up' option or for other groups who were thought to be averse to testing for HIV and therefore more likely to find the features of the swab (such as anonymity, and lack of clinical attendance) more appealing. With HIV testing uptake lower amongst heterosexual men and women than MSM and the highest percentage of late presentation is also seen in this group, and it may be that self-sampling beyond those attending the SH clinic, such as through the THT's online home self-sampling pilot may be the key to increasing HIV testing uptake through self-swab sampling methods in the UK.

Home testing for HIV

With the advent of the availability of home testing for HIV however, many of the problems related to receiving a test result in real time or anxiety over the use of a saliva sample will no longer be an issue as individuals will legally be able to take the test and receive the rapid results themselves, which likely to decrease the need for self-sampling as a means of testing for HIV altogether. As the law on home testing was only changed in April 2014 however, it is still unclear as what the impact of this will be or how it will affect HIV testing practices with no findings from empirical research on this being conducted or published as yet in the UK. Such research would help to clarify the operational and ethical issues associated with home testing for HIV. These issues include, an individuals' ability to effectively preform the test in order to get an accurate result, correctly interpret the result and appropriately respond by seeking out a confirmation of the test result, if positive. There are also many ethical issues posed by the availability of home testing, including the possible impact of the absence of counselling on an individual following a HIV result, whether positive or negative and the possibility of use of coercion to obtain an HIV test result from vulnerable, at risk individuals.

As became apparent in both the DH and the THT pilot projects of home-sampling for HIV, losing contact with those who test positive for HIV infection is likely to be a problem that a safeguard has not been yet developed for.[6,7] There is the risk that the availability of home testing may have no impact in reducing the undiagnosed HIV fraction in the UK, as there is no way of guaranteeing that individuals testing positive will know how, or feel able to seek confirmatory testing and linkage to local HIV care services. Studies assessing entry into HIV care in the United States, following FDA approval of home testing for HIV in 2012 paint a mixed picture of the possible outcomes.[167-169] One review assessing several outcomes of home

testing for HIV, including whether those using home tests were able to effectively perform, obtain accurate results and properly interpret the tests found that individuals struggled with blood collection but that test results and interpretation yielded a high correlation with laboratory and health professional preformed tests.[150] Although they also reported that individuals generally understood the need to confirm a positive test result, there was no data collected as to whether they actually did this following a positive result. A more recent case report of an individual from the US describes the use of the a home HIV test from a trial being used to learn the HIV status of and elicit disclosure from a vulnerable sex partner, and also subsequently found a delay in linking the individual into local HIV care services, illustrating the challenges of the availability of home testing for HIV and the need for ongoing research into outcomes and the requirement of safeguards for the support and protection of home HIV test users.

Limitations

Retention to the pilot was low in this sample with 18% of participants being lost to follow-up and this was detrimental to final results as the total recruited sample size of 50 participants was small. Reasons for this level of loss to follow up may relate to the international nature of clinic attendees with many of those attending GUYS having recently arrived in the UK for a short period and wanting to get a SH whilst living local to the area. Although all participants were asked at recruitment if they were likely to be available for recall at the end of the study year, we are unable to tell whether all those recruited were in the country at the time of recall. There was also a high proportion of DNA, and the reason for this could not be identified but could be related to an anxiety around questions related to sexual behaviour and HIV testing practices in the last year or time constraints. If it is the case, there may a recall bias in our results, with those choosing to attend for an end-of-study recall session having lower risk sexual behaviour and being more likely to have tested for HIV in during the study period.

Overall, the low number of participants who attended for recall may have impacted on our ability to pick up differences in the between group comparisons of HIV testing levels, particularly in assessing differences in HIV testing using the self-sampling swab and sexual risk behaviour as assessed by STI diagnosis levels and number of sexual partners, due to the low level of participants sending in swabs and being diagnosed with STI during the study period, which all 50 participants had agreed to, so it is unlikely that a large number of those lost to follow up would have left the UK altogether. Retention levels were

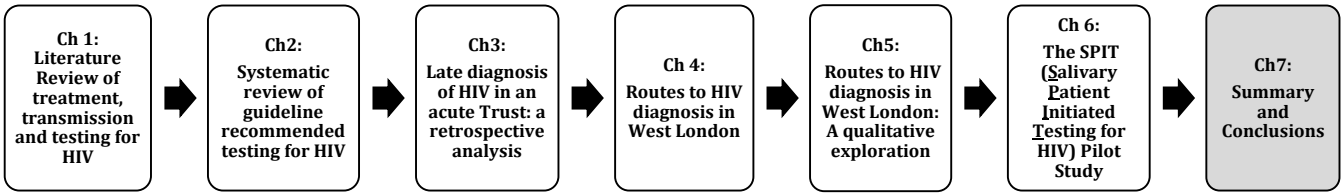
however good enough to identify increases in overall testing levels and in the period before and after recruitment to SPIT and additionally to identify swab samples as the cause of this.

There was no significant difference found in demographic, sexual risk behaviour or HIV testing history in those recruited to SPIT and the wider clinic population, it may well be however that the analysis for this was not sufficiently powered and that this is why no differences were detected. There is also a broader lack of generalisability of these findings to other populations and areas, particularly for other high-risk groups such as heterosexuals from high prevalence countries or those living out of London. For example a qualitative study exploring knowledge and attitudes towards HIV services among African migrants in Britain illustrated institutional issues such as a lack of cultural understanding as a barrier to accessing HIV testing,[24] an aspect not identified amongst this group of SH clinic attending MSM.

CONCLUSION

Despite the low return rate of saliva self-sampling swabs for HIV testing, enrolment into this study did result in an overall increase in repeat rates of HIV testing in this group of young, high-risk MSM, without impacting on sexual risk behaviour. Although respondents found use of the swabs to test for HIV both feasible and acceptable, few participants thought it could be incorporated into their regular SH routine. Their main reasons for this included, length of time to receive results, the isolated HIV testing in the context of overall sexual health, lack of confidence in self-swabbing and validity of results. However, this method of testing for HIV has the potential of having a greater impact on increasing levels of testing in a non-clinic based populations and with the recent approval of self-testing for HIV some of the concerns may be less relevant for future self-testing programs. From our study, there is insufficient evidence that self-sampling should be offered as an alternative to current practice.

Chapter 7: Summary and Conclusions



In this thesis I have explored the barriers to HIV testing in the UK in the era of treatment as a means of preventing HIV transmission. I have done this by assessing the evidence for HIV treatment, reductions in HIV transmission and the role of HIV testing for the reduction in transmission through a literature review on HIV treatment, transmission and testing for HV in the UK (Chapter 1). I have also undertaken a systematic review and meta-analysis of HIV test coverage in the UK in those settings and groups where HIV testing is recommended but where there is no established monitoring system (Chapter 2). I then went on to use routine data collected from patients newly diagnosed with HIV in our local trust (ICHT) to explore demographic characteristics and location of diagnosis and how this was associated with stage of diagnosis (Chapter 3). Following on from this exploration of which patients are diagnosed where and when within our trust, I went on to conduct a mixed methods study, prospectively collecting data on the routes to diagnosis for those newly diagnosed with HIV within the trust over the course of a year; assessing testing behaviours, potential risk behaviours and importantly the attitudes and ideas that inform the patient routes to diagnosis identified previously (Chapters 4 and 5). In Chapter 6 of this thesis I went on to assess the feasibility and acceptability of another model of HIV testing in the UK by undertaking a pilot study for saliva self-sampling to increase repeat testing for HIV among young high-risk MSM. The findings of these investigations are summarised below and the significance of them for HIV testing in the UK is discussed in this chapter.

HIV Treatment and Transmission in the UK

At the start of this thesis I assessed the evidence for treatment as a means of reducing HIV transmission. There is a large body of evidence to support the theory that effective HIV treatment can in itself reduce the risk of transmission of HIV. This evidence ranges from early exploration of the relationship between HIV viral load and the risk of HIV transmission to the efficacy of ART for the significant reduction of viral

load in HIV positive people. I then went on to explore the evidence for effective treatment of HIV positive people and the risk of HIV transmission by assessing studies looking at HIV transmission by several routes, including mother-to-child transmission, needle-stick injury and finally associations in sexual exposure, viral load, ART and the risk of HIV transmission in several RCT. This assessment of studies illustrated that treatment of HIV positive people with ART not only significantly and dramatically reduces morbidity and mortality but by the same process which it achieves this, namely the reduction of the amount of HIV viral copies in the body, also results in a significant reduction in the risk of transmission of the virus.

This reduction in the risk of transmission of HIV is dependent upon several factors which were explored when I went on to assess studies reporting the incidence of observed population level reduction in HIV. Findings from such studies are not clear and several variables are identified as playing an important role in population level reduction of HIV transmission and HIV testing is one of the most important of these. Apart from testing being an essential pre-requisite for the identification of HIV positive persons prior to initiating any treatment, identification of HIV in itself plays an important role in reducing high-risk sexual behaviour contributing to a reduction in HIV transmission. When this evidence is summarised, it becomes clear that early identification of those who are HIV positive is the purpose of HIV testing not only in TAP but also for better outcomes for PLWH.

Early identification of HIV infection is therefore an all-important foundation of both the prevention of onwards HIV transmission and HIV management. Although there have been marked improvements in earlier identification of PLWH in the UK in the last decade, national level data indicates that there not only continues to be a large proportion of people being diagnosed with HIV infection at a late stage of infection (47% in 2012) but also that there continues to be a large fraction of people living with undiagnosed HIV (22%, 95% CI: 18%-27%) in the UK.[68] The routine screening settings that have the highest levels of HIV test offer and uptake are ANC and GUM/SH where 98% and 71% of attendees respectively are tested for HIV. The testing offer and uptake levels are accessible from these settings due to routine surveillance data collected by PHE, and testing in these settings makes up 88% of total HIV test administration in the UK despite routine HIV testing being recommended in a number of other settings.[64] The findings from routine PHE data across the UK illustrates that there is a large proportion of undiagnosed HIV and late diagnosis of HIV in the UK and that this is reflected in apparently poor HIV test coverage in a number of

settings where HIV testing should be routine. Based on this, it is clear that if earlier diagnosis of HIV infection is to be achieved we first require a better knowledge of HIV test coverage across all recommended UK settings and populations and this was the exploration that was undertaken in Chapter 2.

HIV Testing in the UK

In order to assess the level of HIV test coverage in recommended routine screening settings, as defined in the September 2008 BHIVA HIV testing guidelines, I undertook a systematic review of the literature on HIV testing levels in these settings. Studies measuring HIV test coverage in either GUM/SH or ANC settings were not included as these are already surveillance setting for HIV test coverage and the question to be answered was the level of testing undertaken in non-surveillance routine testing settings and populations.

From a search of 1,226 references, 30 studies were identified for inclusion and final data synthesis. These were primary cross-sectional studies or audits of mixed quality coming from published reports, journal articles or conference abstracts. All studies included in final data synthesis quantified the level of HIV testing in a routine guideline recommended group or setting. I chose to stratify the studies by guideline recommended testing setting or population for comparison, either 'Person diagnosed with a disease indicative of possible HIV infection' or 'Persons attending services where routine HIV screening should be undertaken'.

The results of the meta-analysis undertaken showed that estimated HIV test coverage across routine, non-surveillance HIV testing settings is 27.2% (95% CI: 22.4%-32%). This is a conspicuously low level of testing compared to that seen in surveillance settings, suggesting that adherence to September 2008 UK guidelines for HIV testing is poor in these recommended populations and settings. When stratified by group, estimated HIV test coverage in patients diagnosed with a disease indicative of possible HIV infection was 22.4% (95% CI: 13.9%-30.9%) compared to the estimated 29.5% (95% CI: 23.6%-35.4%) in patients attending a routine HIV screening setting. Although the estimated test coverage between the two groups was not significant, the finding of low test coverage in indicator diseases is an important one with routine testing in patients presenting with diseases having been established for many years. The list of indicator nfectious diseases issued in national guidelines were reviewed by a committee of experts on

behalf of the European AIDS Clinical Society (EACS) in advance of the publication of the 2008 guidelines and HIV prevalence in those diagnosed with these diseases was estimated to range between 3% and 94%, with some indicator disease which are highly suggestive of HIV infection being extremely rare, while others having a lower co-prevalence of HIV but being much more common, however recommendations from the panel suggest that even testing a high proportion of individuals with more common disease could have a significant impact on the identification of those with undiagnosed HIV infection. This clearly highlights the importance of indicator disease-guided testing in HIV diagnosis and the potential impact of the finding of low test coverage seen in these group.[90]

A sub-analysis of the 14 studies measuring both level of health care provider test offer to those eligible and patient test uptake was undertaken and the percentage of eligible patients who were offered an HIV test by their health care provider was estimated to be only 40.5% (95% CI: 24.3%-56.7%)whilst the proportion of patients who accepted the offer of an HIV test from their provider was 71.5% (95% CI: 56%-86.9%), indicating that HIV test offer may be more a barrier to overall HIV test coverage than patient test acceptance. This is an issue addressed again later in this thesis where patient attitudes to provider test offer are explored in a cross-section of HIV positive patients from ICHT, participating in the Missed HIV Study. Another important finding to emerge from the systematic review and meta-analysis was the high seroprevalence identified in the studies reporting this information. This was 2.71% (95% CI: 1.05%-4.36%), which is well above the current recommended threshold 0.01% positivity rate, for HIV testing, taken from a US cost-effectiveness analysis.[91, 96]

The overall findings from the systematic review of HIV test coverage in routine non-surveillance settings indicated that test coverage was low and this is likely to be due to low provider test offer more than patient non-acceptance of testing. Findings also indicate that the seroprevalence levels among those tested in these recommended settings is high, indicating that a higher level of testing can also be afforded.

These findings are recognisable within ICHT and patterns in patient diagnosis are likely to correlate with testing coverage. In order to gain a better understanding of what these diagnostic patterns are, and which patients are affected by them in our local area, I undertook an analysis of routine data of patients diagnosed with HIV within the trust over the preceding five-year period in order to explore associations

in demographic characteristics, timing and location of diagnosis for patients diagnosed with HIV in this period.

The findings of this analysis showed that the overall five-year average for the proportion of patients diagnosed with HIV early (that is patients with a CD4 ≥350 cells/mm^3 at the time of diagnosis) is 59.1% of all patients diagnosed within the trust. This proportion of early diagnosis compares favourably with the PHE reported national average of 53%, and also compares well with the London average of 57% for the year 2012.[68] This figure however is not a reflection of the timing of diagnosis of all patients and a regression analysis for demographic characteristics associated with early diagnosis indicated that early diagnosis was significantly less likely in Black Africans compared to other ethnic groups, heterosexuals, compared to MSM and those ≥ 40 years of age compared to those <40 years of age. This pattern of early diagnosis in younger people, non-Black African ethnicities and MSM is also seen at a national level and is an indication that the apparent comparatively high level of early diagnosis of HIV patients in our trust is more likely to be a reflection of the demographic make-up of patients diagnosed within our trust with 66.6% being <40 years of age, 65.4% identifying as MSM and 82.1% of all patients diagnosed over the five-year period being male. Apart from serving as an important reminder that the proportion of early HIV diagnosis alone is not the best indicator of identification of potential undiagnosed infection, it provided a clear picture of the make-up of patients attending our HIV services when planning further investigations in our clinics.

Despite the relative high level of early diagnosis seen within the trust, the change in the proportion of those diagnosed early with HIV has not significantly increased over the 5-year period, indicating that earlier diagnosis of HIV has not improved within in the trust and this is despite an increase in testing initiatives. The settings with the lowest proportion of early diagnosis are those that have previously been associated with having the lowest levels of HIV test coverage. With patients diagnosed in non-routine testing settings found to have an odds of 0.4 (95% CI: 0.3–0.5) of early diagnosis compared to those diagnosed in SH/GUM and ANC settings. The extent of HIV test administration therefore is quite likely to be playing a part in in the time of diagnosis of patients diagnosed with HIV within the trust.

These findings from patients diagnosed within the trust appear comparable to national averages in terms of patterns of diagnosis in timing and location and both the results of the systematic review and of the

analysis of routine clinical data paint an interesting picture of the two sides of HIV diagnosis; illustrating how the patterns seen in test administration nationally are reflected in the patterns seen in patients who are eventually identified as HIV positive locally. There remains however no clear link between these testing patterns and the individual routes of patients later diagnosed with HIV and so I went on to undertake the Missed HIV Study to prospectively investigate the routes to diagnosis of patients newly diagnosed with HIV within ICHT over a 12 month period.

Routes to Diagnosis, Barriers and Facilitators to HIV diagnosis in the UK

A protocol (Appendix J) was drawn up and an application made for ethical approval from the National Research Ethics Service (NRES) to undertaken the 12 month Missed HIV Study. This was a mixed methods study which aimed to investigate the route to diagnosis of patients newly diagnosed with HIV within ICHT through the use of an investigator-led questionnaire and semi-structured interview to assess patient HIV testing history, contact with health services and risk behaviours of those patients.

The results from the quantitative data analysis from the Missed HIV Study provided interesting findings related to patient routes to diagnosis. Among these was the re-appearance in the demographic patterns in diagnosis identified within the trust in Chapter 3 through the questionnaire responses linked to the HIV testing behaviours of patients participating in the study. In response to HIV testing history it was found that both ever having tested for HIV before diagnosis, regular HIV testing (more than once a year) and earlier diagnosis continues to be strongly associated with young gay men with the adjusted odds ratio for ever being tested for HIV before diagnosis being 0.3 (95% CI: 0.4-13.6) in heterosexual men and women compared to MSM and 12.7 (1.2-13) and 8.8 (1.8-42.7) in those in 18-24 and 25-39 years old respectively compared to those ≥50 years of age. Although the lower odds ratio for never having tested for HIV in heterosexuals was not significant, 96.4% of MSM compared to 41.9% of heterosexuals had ever tested for HIV and a greater proportion of MSM also tested for HIV in the 6 months before diagnosis with 29.6% of MSM testing in this time period compared to only 7.7% of heterosexuals.

An interesting finding from the analysis of questionnaire responses to ill health and contact with health care services was that many patients had visited their GP, attended A&E or been admitted to AMU with symptoms that may be suggestive of HIV infection but were not offered an HIV test. In total 39/58 patients (67 %) completing the questionnaire indicated that they had felt symptoms of ill health in the 12

months before HIV diagnosis and had gone to see a health care provider in this period but were not tested for HIV despite being diagnosed with conditions indicative of HIV infection. Seventeen of these patients had also gone for a return visit to their GP, or attended A&E and been admitted to AMU after a second incident of ill health or when their symptoms did not resolve and a total 13 patients were in contact with health care services more than twice in the 12 months before diagnosis and were not offered an HIV test. Furthermore it is unclear exactly how long a period of time many of these patients were suffering symptoms of ill health for or how many times they had gone to see a health care provider in total as responses were only collected for the 12 months preceding diagnosis but findings from interviews indicate that a substantial number were experiencing symptoms of ill health for more than a year before being offered HIV testing and being diagnosed.

Another important finding from the results of the questionnaire was the lack of correlation between HIV testing and reported sexual risk behaviour. There was no significant association found between having a casual sexual partner, having a sexual partner who is born in a country of high prevalence, or even having a known HIV positive partner in the 12 months before HIV diagnosis and having an HIV test in that time period. There was also no significant association found between the total numbers of casual sexual partners where UVA occurred in the 6 months before diagnosis and testing for HIV in the same period. Although, this may be due to a lack of power to detect such an association in our study, the association between risk behaviour and HIV testing and lack of correlation between these emerges as an important theme when explored as part of the qualitative analysis in this study, and again in the findings from semi-structured interviews among young, high-risk MSM in our home self-sampling for HIV pilot where many participants report a risk-based testing approach to their HIV testing practices but underestimate the level of risk in their sexual behaviour.

Risk-based testing is in theory a good method for HIV testing; patients who have engaged in some form of high-risk sexual behaviour such UAV go to visit their GP or attend the GUM/SH clinic in order to request an HIV test. The problem with this method of HIV testing, as indicated by the findings from the questionnaire is that most patients citing this as an HIV testing practice report high-risk sexual behaviour but do not follow this up with and an HIV test. Some of the possible reasons for this emerged from interviews with participants and in older participants (particularly older MSM), a lack of 'current risk' was cited as a reason for not testing despite a history of more high-risk sexual behaviour in the past and

no testing for HIV subsequent to this period. In other, younger, participants explaining their testing practices there is an apparent low perceived self-risk despite clearly reporting high-risk sexual behaviours such as UVA with multiple casual partners. This does not seem to be due to lack of knowledge of HIV but rather due to a moderation in the association between HIV knowledge and sexual risk behaviour. Some studies indicate that negative HIV tests may also be contributing to this, resulting in patients downgrading the risks they take in future and therefore reducing the frequency of HIV testing.[170-172] These findings quite clearly highlight the degree of this lack of congruence between self-perceived risk and actual risk but also and more importantly highligh how patient-initiated testing, particularly risk-based testing, can be an ineffective form of HIV testing.

One strong and positive theme to emerge from the results of the semi-structured interviews was that many patients reported incorporating testing for HIV into their sexual health or health routine, these were often participants who regularly tested for HIV and had all had at least one HIV test in the 12 months preceding HIV diagnosis. Those testing in this manner cited feelings of responsibility for their own health and the sexual health of others as a reason for this practice and many also expressed that they had become accustomed to regular attendance to the sexual health clinic making it an essential part of their routine. The issue that emerged with this however was that this sense of familiarity and routine was not felt by all participants with some, particularly heterosexual men, expressing a strong feeling of unease and stigma in attending the sexual health clinic. For some participants this feeling was overwhelming, and was enough to discourage some from regular attendance as many felt that they could not identify with other attendees to the clinic and did not consider it a place suitable for themselves despite their having been at risk and tested positive for HIV, exactly like other clinic attendees. Accounts of reflected self-stigma were not the only experiences of stigma expressed with some participants also citing examples of feeling stigmatised due to health care provider attitudes to suspicions of HIV infection in patients, with some participants expressing apparent health care provider embarrassment and instances where they were not tested for HIV but referred to other clinics instead. This not only resulted in feelings of anxiety and shame in patients but also delayed and could have potentially prevented diagnosis.

Frustration with some health care providers encountered was a strong theme among some participants completing semi-structured interviews, particularly those who had the most contact with health care providers due to long periods of ill health. It may be that many of these feelings have arisen in retrospect

of diagnosis and improvements in symptoms, causing patients to report their interactions with doctors and nurses before diagnosis in a highly biased way and some patient did appear to be associating their HIV consultant with the improvement in their symptoms and comparing this to their GP and other specialists who were unable to help resolve their symptoms. However much of the feeling of frustration seemed to be clearly associated with the ill health itself and feelings of annoyance, bordering on anger emerged later, after diagnosis when patients reflected on why they had not tested for HIV before. Deference to their doctors and nurses was common in these patients and this seemed to justify the anger they felt subsequently as they had little or no part to play in their diagnosis and the responsibility for it was solely down to the health care providers involved in their care.

Although there were challenges in achieving a sample size large enough to detect potential differences in testing behaviours and timing of HIV diagnosis as well as difficulties in sampling women and people of Black African ethnicity for interview, the findings from the Missed HIV Study highlighted important factors associated with HIV diagnosis of patients in ICHT. Routes to HIV diagnosis are highly variable among patients and these are a reflection of not only the HIV testing practices of the individual patient, but also the testing practices of their health care providers, particularly in those experiencing ill health in the run up to HIV diagnosis. The differences in attitudes to and motivations for HIV testing are among the factors that shape the demographic differences seen in location and timing of patients' diagnosis. As indicated by the results of the systematic review earlier in the thesis testing for HIV, particularly among those patients presenting with conditions that may be indicative of HIV infection is poor and in those who are not 'routine testers' patient risk-based testing practices are ineffective for adequate and timely identification of HIV infection. The results of patient routes to diagnosis indicate that the barriers to HIV testing experienced are not ones that can be overcome on an individual patient level and that there is a real requirement for increased provider testing. The role of the clinician in testing for HIV has become more, not less important in an era of ART. With a decreased morbidity and mortality, and reduction in transmission risk there is a need for a change in culture towards HIV testing, which is most easily and potentially most effectively, initiated in clinical settings. If testing for HIV cannot be made a normal process for clinicians, it leaves little hope for the idea of normalisation of testing among individual patients and the public and so further exploration of the system increase required to facilitate this change in HIV testing among clinicians should be the primary aim in future HIV testing research.

As a follow up to the findings from the patient aspect of the Missed HIV study a further questionnaire was designed and sent out to a group of health professionals in order to gauge the extent of provider knowledge of testing and patterns in provider practice and to what extent this may be contributing to patterns in diagnosis identified and explore which methods may be used to improve testing behaviours. The results of this work have been collated but have not yet been analysed so could not be added to this thesis. A project is currently underway to analyse this data and further explore provider patterns and attitudes in test offer qualitatively from March 2015.

Home Testing and Beyond – The Future of HIV testing in the UK

Much HIV testing research in recent years has been towards models of community based and home sampling for HIV. Recommendation from NICE [69, 70] and BHIVA[64] encourage interventions to increase HIV testing outside of clinical settings including several pilots of expanded testing interventions, including pop-up clinics for HIV testing and general health screen targeting of high-risk groups.[55] This increased focus on out of clinic testing for HIV and STI, is not always found to be appropriate[157, 167] and such interventions can be fraught with issues related to lack of patient follow up resulting in challenges in test result confirmation and linkage to specialist health services.[134] There is a risk that research focused exclusively on these programmes may have adverse effects on the culture of HIV testing in the clinic by drawing testing outside of clinical settings and exclusively targeting specific high-risk groups they may act to dilute the message of routine HIV testing in recommended clinical settings, which is already a challenge.[170, 171] However, the value of these programmes for accessing hard-to-reach groups who are not in routine contact with health services or high-risk groups where regular HIV testing is recommended is of course immense and as such, they are likely contribute to increases in HIV diagnosis beyond current levels.[69, 70]

In order to gauge the extent of this benefit in increasing HIV testing and to assess some of the issues that may be raised with the advent of HIV home testing, I went on to undertake a pilot study for the feasibility and acceptability of home based salivary self-sampling for HIV among high-risk MSM attending a dedicated young gay men's sexual health clinic in West London.

The SPIT study was a mixed method, 12-month observational study which assessed level of saliva self-sampling for HIV testing in MSM between May 2012 and April 2013. The primary outcome of the study

was the difference in HIV test uptake before and after the availability of self-sampling swabs. Secondary outcomes were number of swabs used for HIV self-sampling and the number of positive HIV results (and linkage to specialist care for confirmatory testing in reactive samples). At the start of the study 50 young MSM were recruited to SPIT and were provided with swabs for self-sampling for HIV along with instructions on sample collection and return. Participants also completed baseline questionnaires on prior HIV testing. Salivary self-swab samples which were sent in were tested for HIV over the course of the year and results were returned to participants via their chosen method of contact (text, phone call or email). 12 months later, participants were invited to a recall appointment to complete an end-of-study questionnaire on HIV testing and some were also invited to take part in semi-structured interviews on their experiences testing for HIV and using the salivary self-swab as a means of testing for HIV.

Results showed that although the average level of HIV testing increased from baseline within the group by 1 test per participant, self-swab sample return rate was low with only 30% of participants sending in a swab sample for HIV testing over the 12 month period. One participant recruited to SPIT also had a reactive HIV POCT during the study period at a SH clinical attendance but did not send in a saliva swab sample at all. This participant was also subsequently lost to follow-up, not returning for confirmatory testing. Although this positive test result was not related to the study, it serves as a reminder of the difficulty in linking patients to care, even when they receive a positive HIV test within a clinical setting.

The findings from the semi-structured interviews gave a clear indication of why SPIT study participants had a low uptake of the self-sampling swabs. All participants who were interviewed indicated that they did not use the swab at all or only occasionally because they were themselves already attending the sexual health clinic regularly and many of those returning a sample stated that they completed one for the experience of self-sampling rather than due to feeling the need for an HIV test. This result is somewhat unsurprising as all participants were recruited from a dedicated 'late opening' gay men's sexual health clinic, where they were already in regular attendance and were comfortable and confident in the sexual health service provided there, preferring it to isolated testing for HIV. Despite this most participants did express that they liked having the option of self-sampling as a means of testing for HIV and also indicated that it was likely to be a more appealing option to those who were not regular SH clinic attendees or disliked conventional means of testing for HIV (e.g. those who dislike needles).

The change in the law allowing HIV testing to become available to members of the general public in April 2014 is likely to mean that much of what was useful in the home self-sampling method of HIV testing may now be redundant. The implications of the findings of the SPIT study are however interesting in the context of the recent advent of home testing for HIV in the UK. Although many of the factors that may have had an impact on the low uptake of self-sampling for HIV testing may not be the same for home testing (e.g. results of tests are received immediately and, in most cases, home testing will not require any attendance to a clinic to collect the test but will be more likely to be available to order from home)[134] there are some challenges identified that are likely to also be seen in home testing, particularly issues in accurate interpretation of test results and appropriate responses to reactive HIV test results and these have also been assessed as possible contributors to delays in home testing in the US.[167-169, 172] Challenges such as these along with those more unique to home testing such as the potential for use of coercion in testing partners or vulnerable people for HIV,[168] highlight the need for on-going research and monitoring of home testing for HIV. Currently, due to the relatively recent change in the law and lack of availability of an approved HIV test for UK use, no studies have been published which have assessed these outcomes in the UK. These are essential to inform the development of effective HIV home testing intervention programmes, with safeguards to reduce the potential adverse consequences of this method of testing. Although the advent of home testing for HIV holds many unknown outcomes and much potential for the identification of PLWH it will not in itself be a panacea for challenges in identification of HIV in the UK.

Conclusions

Current testing practices are not enough to achieve equitable access to early diagnosis for HIV. Testing practices of clinicians, along with system challenges play an important role in HIV testing and changing these may be the most effective method of increasing earlier identification of HIV positive individuals in the UK.

Patient routes to HIV diagnosis are complex and have demographic associations which differentiate HIV testing and diagnosis patterns along the lines of age and ethnicity but also and more clearly between MSM and heterosexuals and as such testing interventions should be focused to target these differences appropriately. However targeted testing of these groups or provider-biased testing has often been ineffective and this appears to be the problem with testing in clinical settings currently. The most

effective way to increase testing in target groups is likely to be more routine testing; applying the recommended standard to HIV testing among all clinicians will have an important impact in reducing undiagnosed HIV and increasing earlier testing in these groups.

Although expanded community testing and home testing for HIV will have increasingly important roles to play in earlier testing for HIV and are likely to significantly contribute to improvements in the identification of HIV in future, improved testing will only truly be achieved with a change in the attitudes and culture of HIV testing among both patients and clinicians. Changing clinician testing patterns in particular is likely to be the simplest and most effective first step in doing so. A better understanding of the system changes that can be made to support clinicians and facilitate an increase in routine HIV testing in recommended settings is of great importance in the future and this will be the focus of my future research as the next step in improving HIV testing in the UK.

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Appendices

Appendix A: Adherence to guideline recommended HIV testing in non-specialist clinical settings: Protocol

Title

Adherence to guideline recommended HIV testing in non-specialist clinical settings

Question

To what extent are guideline recommendations for routine testing for HIV adhered to outside of Genitourinary, Sexual Health and HIV clinics and antenatal settings (specialist settings)?

Background

Implementation of HIV testing in the UK

An estimated 91,500 people were living with HIV in the UK in 2010 and almost a quarter of these people were unaware of their HIV-positive status, increasing their risk of transmitting the virus onto others and presenting to healthcare services later in infection. In the same year 50% of total new HIV diagnoses made were at a clinically late stage of infection (CD4 cell count of <350 cells/mm^3) with these patients experiencing a higher risk of developing an (Acquired Immunodeficiency Syndrome) AIDS defining condition and ten-fold increased risk of death within a year of diagnosis. Timely identification of those who are HIV positive and appropriate referral into care services is therefore essential in the reduction of both HIV associated morbidity and mortality and prevention of HIV transmission and the high rates of undiagnosed HIV infection and late presentation reported in the UK are a reflection of inadequate rates of HIV testing.

Currently, there is routine monitoring of national levels of HIV testing through estimations generated from sentinel Genitourinary (GUM), Sexual Health (SH) and HIV clinics and antenatal care settings data however, it is in these setting that we find the highest levels of HIV testing with rates in 2010 at 69% in

GUM/SH clinic attendees and 96% in antenatal care clinic attendees; accounting for 47% and 31% of total HIV tests in the UK, respectively.

The latest national guidelines on HIV testing* were published in October 2008. The guidelines were published by BHIVA and written in collaboration with the BIS and the BASHH. These guidelines were intended to prompt an increase in HIV testing in all healthcare settings in order to reduce the proportion of individuals with undiagnosed HIV infection. The authors of the guidelines state the reason for the need of their publication as being a) misconceptions regarding HIV testing remaining a hindrance to increased testing; b) the importance of both the individual patient and public health benefits of increased testing and c) the need for up-to-date guidance that would enable any clinician to perform an HIV test within good clinical practice, thereby encouraging the 'normalisation' of HIV testing.

Objectives

To assess adherence to 2008 BHIVA guideline recommended testing outside of GUM/SH/ HIV clinics and antenatal care settings.

Population

People eligible for HIV testing according to the 2008 national guidelines and excluding those already known to be HIV positive or attending a GUM/SH/HIV clinics or antenatal care setting.

Outcome Variables

Number of HIV tests received by people eligible for HIV testing

The number of HIV tests offered to those eligible for HIV testing

The number of positive HIV test results in those tested

Time Period

Only studies where data collection commenced after publication of 2008 guidelines will be included.

Linguistic range

Only studies with UK based sites or settings will be included for review. Only studies identified in English will be used as the review topic is exclusive to UK practice and there is therefore unlikely to be any selection bias as a product of this.

Design and Method

Due to the nature of the study question a range of study designs and methodologies may be used to assess the outcomes specified and therefore all study designs and methodologies will be included and the quality of these will be assessed individually in the review.

Eligibility Criteria	**Inclusion**	**Exclusion**
Intervention	All studies measuring HIV testing in recommended settings	Any trial of new HIV test
Setting	Recommended testing settings only	Studies exclusively measuring testing levels in routine GUM/SH/HIV clincs or antenatal care settings
Population	All patients recommended for HIV testing according to 2008 BHIVA guidelines	HIV positive patients Health providers working exclusively in GUM, Sexual Health, HIV clinics or Antenatal care settings
Outcome	Number of HIV tests received by people eligible for HIV testing The number of HIV tests offered to those eligible for HIV testing The number of positive HIV test results in those tested	

Time Period	Commenced post 2008 (post national HIV testing guidelines publication)	Studies without HIV testing for the period after September 2008
Linguistic range	English language articles	
Design and Method	All studies with quantitative methods of analysis	Exclusively qualitative research studies
Sample size and response rate	All sample sizes and response rates	

Table 1: Inclusion and exclusion criteria for study selection

Search strategy

Databases

MEDLINE, Embase, HMIC, PsycINFO and conference abstracts will be searched for studies (via Ovid).

Search period

Databases will be searched from September 2012 to December 2012 (date of final review article compilation). An additional one-off search in February 2013 to screen for recently published articles.

Search term concepts

HIV **OR** Human immunodeficiency virus

test/tests/testing

United Kingdom **OR** UK **OR** England **OR** Northern Ireland **OR** Scotland **OR** Wales

Search term combinations

To identify studies that address the question of extent of implementation of national HIV testing guidelines, search terms**1 AND 2 AND 3** will be entered into database search engines.

Extended search

In order to identify all potential data for the review, reference lists for all studies generated from initial search and inclusion of databases using search terms detailed will also be retrieved for assessment under eligibility criteria and inclusion in the review.

Elimination of studies that do not meet inclusion criteria or do meet exclusion criteria

After generation of initial bibliography from search strategy, candidate studies will be excluded after 1) screening of titles and abstracts 2) screening of whole article.

Extraction

Exposure group/Risk group – Which risk of HIV exposure do the study population fall under

Primary testing outcome - Which is the primary outcome related to HIV testing in the study

Exclusion – Which individuals have been excluded from the study

Time period (date) -The duration of the study and time which it took place

Population – Who was asked to participate in the study

Location (Diagnosed HIV prevalence per 1,000 15-59 year olds) – Location that the study was conducted in and local area diagnosed HIV prevalence as indicated by HPA SOPHID data, 2009.

Number of settings/centres – The number of centres in which participants were recruited or chosen from

Type of setting/centre – The type of clinical setting this was

Design – The design of the study

Reporting/recording method of primary testing outcome - Instrument used to measure the primary testing outcome

Number eligible to test – The number of people identified as eligible to test

Number offered test – The number of people offered a test

Number tested – The number actually tested

Proportion of tested (%) – The percentage of those eligible to test who test for HIV

Proportion testing positive – The percentage of those tested who are HIV-positive

Where HIV testing was measured in the same population in different time periods the most recent records of testing levels were extracted.

***Recommendations for testing**

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

1. GUM or sexual health clinics

2. antenatal services

3. termination of pregnancy services

4. drug dependency programmes

5. healthcare services for those diagnosed with tuberculosis, hepatitis B, hepatitis C and lymphoma.

B. An HIV test should be considered in the following settings where diagnosed HIV prevalence in the local population (PCT/LA) exceeds 2 in 1000 population:

1. all men and women registering in general practice

2. all general medical admissions.

C. HIV testing should be also routinely offered and recommended to the following patients:

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

1. all patients presenting for healthcare where HIV, including primary HIV infection, enters the differential diagnosis

2. all patients diagnosed with a sexually transmitted infection

3. all sexual partners of men and women known to be HIV positive

4. all men who have disclosed sexual contact with other men

5. all female sexual contacts of men who have sex with men

6. all patients reporting a history of injecting drug use

7. all men and women known to be from a country of high HIV prevalence (>1%*)

8. all men and women who report sexual contact abroad or in the UK with individuals from countries of high HIV prevalence

D. HIV testing should also be routinely performed in the following groups in accordance with existing Department of Health guidance:

1. Blood donors

2. Dialysis patients

3. Organ transplant donors and recipients.

Appendix B: Complete STATA command code for meta-analyses and sensitivity analysis

Written by Sarah Gerver and Gabriella Gomez, adapted by Rahma Elmahdi

```
use "C:\Users\Rahma Elmahdi\Desktop\Review\reviewmetaanaly\FinalMetanData.dta"

lab define group 0"Persons diagnosed iwth diseaseindicative of HIV infection" 1"Persons attending a service where routine HIV screening is undertaken (excluding SH/HIV/ANC)"

lab values group group

tab group

lab define testtype 0"POCT" 1"blood" 2"Unspecified"

lab values testtype testtype

tab testtype

lab define opt 0"Opt-in" 1"Opt-out" 2"Unspecified"

lab values opt opt

lab define delivery 0"standard" 1"staff education" 2"HIV specialist"

lab values delivery delivery

tab delivery

lab define location 0"London" 1"Not London"

lab values location location

tab location

lab define studytype 0"retrospective" 1"prospective"
```

```
lab values studytype studytype

tab studytype

gen proptest = .

gen proptestuci = .

gen proptestlci = .

forv i =1(1) 30 {

cii eligible[`i'] tested[`i']

 qui replace proptest = r(mean) in `i'

 qui replace proptestuci = r(ub) in `i'

 qui replace proptestlci= r(lb) in `i'

 }

gen percenttest = proptest*100

gen percenttestuci = proptestuci *100

gen percenttestlci = proptestlci *100

metan percenttest percenttestlci percenttestuci, random lcols(Study) xlabel (0,100) nulloff effect
("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive
a test, size (vsmall) color(black) position(6)) astext(80)

metan percenttest percenttestlci percenttestuci, random lcols(Study) by(group) xlabel (0,100) nulloff
effect ("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to
receive a test, size (vsmall) color(black) position(6)) astext(80)

metan percenttest percenttestlci percenttestuci, random lcols(Study) by(opt) xlabel (0,100) nulloff effect
("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive
a test, size (vsmall) color(black) position(6)) astext(80)
```

metan percenttest percenttestlci percenttestuci, random lcols(Study)by(testtype) xlabel (0,100) nulloff effect ("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive a test, size (vsmall) color(black) position(6)) astext(80)

metan percenttest percenttestlci percenttestuci, random lcols(Study) by(delivery) xlabel (0,100) nulloff effect ("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive a test, size (vsmall) color(black) position(6)) astext(80)

metan percenttest percenttestlci percenttestuci, random lcols(Study) by(location) xlabel (0,100) nulloff effect ("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive a test, size (vsmall) color(black) position(6)) astext(80)

metan percenttest percenttestlci percenttestuci, random lcols(Study) by(studytype) xlabel (0,100) nulloff effect ("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive a test, size (vsmall) color(black) position(6)) astext(80)

metan percenttest percenttestlci percenttestuci if testtype !=2, random lcols(Study)by(testtype) xlabel (0,100) nulloff effect ("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive a test, size (vsmall) color(black) position(6)) astext(80)

metan percenttest percenttestlci percenttestuci if opt !=2, random lcols(Study)by(opt) xlabel (0,100) nulloff effect ("Percentage tested") label(namevar=Study) title(Percentage of patients eligible for HIV testing to receive a test, size (vsmall) color(black) position(6)) astext(80)

gen logoddsproptest = log(proptest/(1-proptest))

gen selogoddsproptest= sqrt(1/eligible*proptest)+(1/(eligible*(1-proptest)))

xi: metareg logoddsproptest i.group, wsse(selogoddsproptest) eform

xi: metareg logoddsproptest i.location, wsse(selogoddsproptest) eform

xi: metareg logoddsproptest i.testtype, wsse(selogoddsproptest) eform

xi: metareg logoddsproptest i.delivery, wsse(selogoddsproptest) eform

xi: metareg logoddsproptest i.opt, wsse(selogoddsproptest) eform

```
xi: metareg logoddsproptest i.studytype, wsse(selogoddsproptest) eform

xi: metareg logoddsproptest i.studytype if group==1, wsse(selogoddsproptest) eform

gen propoffer =.

gen propofferuci =.

gen propofferlci=.

drop if offer == .

forv i=1(1)30 {

cii eligible[`i'] offered[`i']

 qui replace propoffer=r(mean) in `i'

 qui replace propofferuci=r(ub) in `i'

 qui replace propofferlci=r(lb) in `i'

 }

gen percentoffer = propoffer*100

gen percentofferuci = propofferuci * 100

gen percentofferlci = propofferlci*100

metan percentoffer percentofferlci percentofferuci, random lcols(Study) xlabel(0, 100) nulloff
effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible offered HIV
testing, size (vsmall) color (black) position(6)) astext(80)

metan percentoffer percentofferlci percentofferuci, random lcols(Study) by(testtype) xlabel(0, 100)
nulloff effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible
offered HIV testing, size (vsmall) color (black) position(6)) astext(80)
```

```
metan percentoffer percentofferlci percentofferuci, random lcols(Study) by(opt) xlabel(0, 100) nulloff effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible offered HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentoffer percentofferlci percentofferuci, random lcols(Study) by(delivery) xlabel(0, 100) nulloff effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible offered HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentoffer percentofferlci percentofferuci, random lcols(Study) by(location) xlabel(0, 100) nulloff effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible offered HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentoffer percentofferlci percentofferuci, random lcols(Study) by(studytype) xlabel(0, 100) nulloff effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible offered HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentoffer percentofferlci percentofferuci if testtype != 2, random lcols(Study) by(testtype) xlabel(0, 100) nulloff effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible offered HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentoffer percentofferlci percentofferuci if opt != 2, random lcols(Study) by(opt) xlabel(0, 100) nulloff effect("Percentage offered testing") label(namevar=Study) title(Percentage of those eligible offered HIV testing, size (vsmall) color (black) position(6)) astext(80)

gen propaccept =.

gen propacceptuci=.

gen propacceptlci=.

forv i=1(1)30 {

cii offered[`i'] tested[`i']

qui replace propaccept=r(mean) in `i'

qui replace propacceptuci=r(ub) in `i'
```

```
qui replace propacceptlci=r(lb) in `i'

}

gen percentaccept = propaccept*100

gen percentacceptuci = propacceptuci * 100

gen percentacceptlci = propacceptlci*100

metan percentaccept percentacceptlci percentacceptuci, random lcols(Study) xlabel(0, 100) nulloff
effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those offered who
accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentaccept percentacceptlci percentacceptuci, random lcols(Study) by(testtype) xlabel(0, 100)
nulloff effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those offered who
accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentaccept percentacceptlci percentacceptuci, random lcols(Study) by(opt) xlabel(0, 100)
nulloff effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those offered who
accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentaccept percentacceptlci percentacceptuci, random lcols(Study) by(delivery) xlabel(0, 100)
nulloff effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those offered who
accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentaccept percentacceptlci percentacceptuci, random lcols(Study) by(location) xlabel(0, 100)
nulloff effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those offered who
accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentaccept percentacceptlci percentacceptuci, random lcols(Study) by(studytype) xlabel(0,
100) nulloff effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those
offered who accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)
```

```
metan percentaccept percentacceptlci percentacceptuci if testtype!=2, random lcols(Study) by(testtype) xlabel(0, 100) nulloff effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those offered who accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)

metan percentaccept percentacceptlci percentacceptuci if opt != 2, random lcols(Study) by(opt) xlabel(0, 100) nulloff effect("Percentage accepting testing") label(namevar=Study) title(Percentage of those offered who accepted HIV testing, size (vsmall) color (black) position(6)) astext(80)

clear

import excel "C:\Users\Rahma Elmahdi\Desktop\appendixb.xlsx", sheet("Sheet1") firstrow

lab define group 0"Persons diagnosed iwth diseaseindicative of HIV infection" 1"Persons attending a service where routine HIV screening is undertaken (excluding SH/HIV/ANC)"

lab values group group

tab group

lab define testtype 0"POCT" 1"blood" 2"Unspecified"

lab values testtype testtype

tab testtype

lab defin opt 0"Opt-in" 1"Opt-out" 2"Unspecified"

lab values opt opt

lab define delivery 0"standard" 1"staff education" 2"HIV specialist"

lab values delivery delivery

lab define location 0"London" 1"Not London"

lab values location location

tab location

lab define studytype 0"retrospective" 1"prospective"
```

```
lab values studytype studytype

tab studytype

drop if seropositive==.

gen proppos =.

gen propposuci=.

gen propposlci=.

forv i=1(1)24 {

cii tested[`i'] seropositive[`i']

qui replace proppos=r(mean) in `i'

qui replace propposuci=r(ub) in `i'

qui replace propposlci=r(lb) in `i'

}

gen percentpos=proppos*100

gen percentposuci=propposuci*100

gen percentposlci=propposlci*100

metan percentpos percentposlci percentposuci, random lcols(Study) xlabel(0,5, 10) nulloff
effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size
(vsmall) color (black) position(6)) astext(80)

metan percentpos percentposlci percentposuci, random lcols(Study) by(GROUP)  xlabel(0,5, 10) nulloff
effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size
(vsmall) color (black) position(6)) astext(80)
```

metan percentpos percentposlci percentposuci, random lcols(Study) by (opt) xlabel(0,5, 10) nulloff effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size (vsmall) color (black) position(6)) astext(80)

metan percentpos percentposlci percentposuci, random lcols(Study) by(testtype) xlabel(0, 5, 10) nulloff effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size (vsmall) color (black) position(6)) astext(80)

metan percentpos percentposlci percentposuci, random lcols(Study) by(delivery) xlabel(0, 5, 10) nulloff effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size (vsmall) color (black) position(6)) astext(80)

metan percentpos percentposlci percentposuci, random lcols(Study) by(location) xlabel(0, 5, 10) nulloff effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size (vsmall) color (black) position(6)) astext(80)

metan percentpos percentposlci percentposuci, random lcols(Study) by(studytype) xlabel(0, 5, 10) nulloff effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size (vsmall) color (black) position(6)) astext(80)

metan percentpos percentposlci percentposuci if opt !=2, random lcols(Study) by(opt) xlabel(0, 5, 10) nulloff effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size (vsmall) color (black) position(6)) astext(80)

metan percentpos percentposlci percentposuci if testtype !=2, random lcols(Study) by(testtype) xlabel(0, 2, 4, 6, 8, 10, 12) nulloff effect("Percentage testing positive") label(namevar=Study) title(Percentage testing seropositive, size (vsmall) color (black) position(6)) astext(80)

log close

Appendix C: Complete data tables for final studies identified for inclusion

Study	Title	Article	Primary testing outcome	Exclusions	Time period (duration)	Population	Number of centres	Type of centre	Measure/reporting method
Persons diagnosed with a disease indicative of possible HIV infection									
Gupta, N.D. & Lechelt, M. (2011)	**Assessment of the implementation and knowledge of the UK national guidelines for HIV testing (2008) in key conditions at a UK district general hospital**	Yes - Audit Report	Electronic departmental record or HIV testing and Electronic pathology records	Non-verifiable data	August 2009 – June 2012 (11 months)	Inpatients at Basildon & Thurrock Hospital	1	Secondary care hospital	Electronic record of HIV test

Thomas William, S., *et al.* (2011)	**Changes in HIV testing rates among patients with tuberculosis in a large multi-ethnic city in the UK**	Yes - Audit Report	Laboratory database record of HIV test	<18 years, private patients, chemoprophylaxis patients, non-tuberculosis mycobacteria, diagnosis outside catchment area	September 2008 – March 2009 (6 months)	Patients registered on the Birmingham Tuberculosis aftercare register	>1	Various	Laboratory record of HIV test
Hsu, D., *et al.* (2012)	**Diagnosing HIV infection in patients presenting with glandular fever-like illness in primary care: are we missing primary HIV infection?**	Yes - Short Communication	Record of HIV test	Not reported	April 2009 - June 2010 (14 months)	Primary care patients in Lambeth and Southwark	72	Primary care clinics	Laboratory record of HIV test request

Page, I., *et al.* (2011)	**The impact of new national HIV testing guidelines at a district general hospital in an area of high HIV seroprevalence**	Yes - Paper	Laboratory record of HIV test	HIV test requests from GUM clinics	October 2008 – September 2009	Inpatients in Blackpool	1	Secondary care hospital	Laboratory record of HIV test
Thomson-Glover, R., *et al.* (2011)	**Diagnosing HIV in non-GUM secondary care settings**	No - Abstract	Record of HIV test	not reported	November 2009 - April 2010 (6 months)	inpatients Warrington & Halton hospitals	2	Secondary care hospitals	Record of HIV test
Thorburn, F. (2012)	**The impact of a multi-disciplinary meeting on the rates of HIV in testing in TB patients**	No - Abstract	Record of HIV test offer	not reported	2010 - 2011 (duration not reported)	Tuberculosis patients attending virology centre in Glasgow	1	Tertiary care clinic	Laboratory record of HIV test administration

Vas, A., *et al.* (2012)	**HIV testing and in TB and Hepatitis services in a district general hospital**	No - Abstract	Record of HIV test	not reported	2009 (duration not reported)	Indicator disease patients in a Manchester hospital	1	Secondary care hospital	Record of HIV test administration
Byrne, L., *et al.* (2011)	**HIV specialists must lead the way to make HIV testing truly routine**	No-Abstract	Record of HIV test	, <18, non-medical specialty, underlying chronic lung disease, hospital-acquired pneumonia	February - April 2010 (3 months)	Patients admitted with community-acquired pneumonia	1	Acute medical admissions unit	Case-note record of HIV test administration
Persons attending services where routine HIV screening should be undertaken									
Chan, S.Y., *et al.* (2011)	**Acceptance of HIV testing in medical inpatients: A local acceptability study**	Miscellaneous	Consent to have an HIV test	<15 and >59 years, total time admitted <24 hours, assessed as unable to consent, known to be HIV-positive	September 2009 (2 weeks)	Acute medical admissions in Croydon	1	Acute medical admissions unit	Offer and acceptance of HIV test

Rayment, M., *et al.* (2012)	**HIV Testing in Non-Traditional Settings - the hints study: A multi-centre observational study of feasibility and acceptability.**	Article	Offer of HIV test to eligible individual	<16, >65 years, known HIV positive, not accessing healthcare for the first time in testing period, not able to consent	January – September 2010 (12 weeks each site)	Patients attending primary and secondary healthcare services in 4 London centres	4	Acute care units, Dermatology OPD	Administration of HIV oral fluid or 4th generation HIV serology
Perry, N. *et al.* (2011)	**HIV testing in acute general medical admissions must be universally offered to reduce undiagnosed HIV**	Abstract	Record of HIV test	<16 and >79 years, known HIV positive	August 2009 – January 2010 (5 months)	Acute medical admissions in Brighton	1	Acute medical admissions unit	HIV test result
Bryce, G. (2009)	**A study to assess the acceptability, feasibility and**	Abstract	Acceptance of HIV test offer	<16 and >59 years	May - November 2010 (4 months)	Patients attending primary care	9	Primary care clinics	HIV POCT test

	cost-effectiveness of universal HIV testing with newly registering patients (aged 16-59) in primary care					services in Brighton			
Ashby, J., *et al.* (2012)	**HIV testing uptake and acceptability in an inner city polyclinic**	Article	Acceptance of HIV test offer	<16, >65 years, unable to consent	2011 dates not specified (random 4-hour duration over a 4 week period)	Polyclinic attendees in west London	1	Polyclinic	Rapid point-of-care HIV test
Ellis, S., *et al.* (2011)	**Offering HIV testing in an acute medical admissions unit in Newcastle upon Tyne**	Clinical Medicine research	Record of HIV test	<18 years, no capacity for consent	September - October 2009 (11 weeks) and January - March 2010 (6 weeks)	Acute medical admissions in Newcastle	1	Acute medical admissions unit	HIV test offer and administration

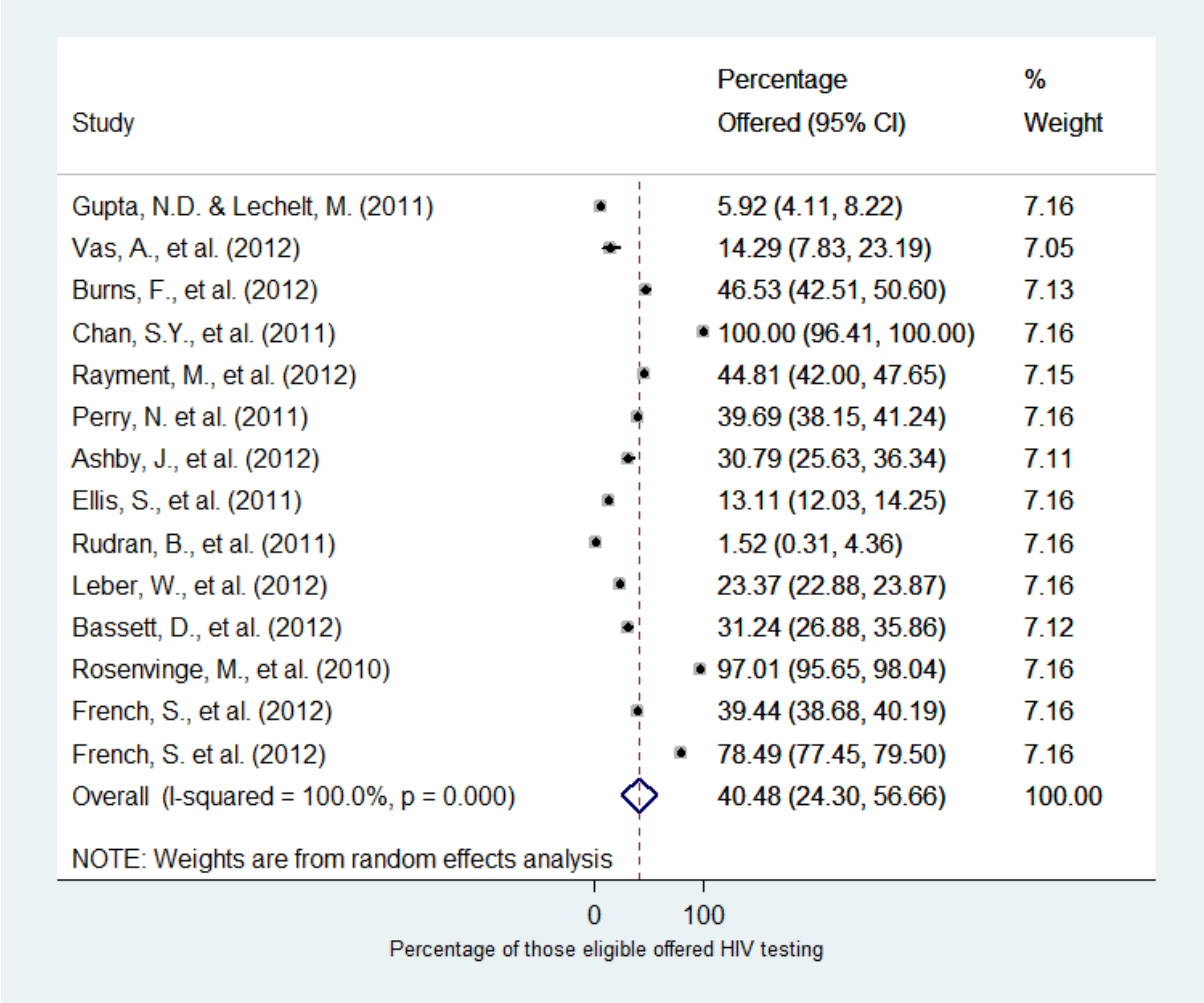
Rudran, B., *et al.* (2011)	**HIV testing in acute medical admissions**	Abstract	Record of HIV test	not reported	2010 - exact date not specified (1 week)	Acute medical admissions in Bournemouth	1	Acute medical admissions unit	Hospital or laboratory database record of HIV test
Leber, W., *et al.* (2012)	**Can point-of-care HIV testing in primary care increase identification of HIV? The RHIVA 2 Cluster randomised control trial - update**	Abstract	Offer of rapid point-of-care HIV test	<16 years,	May 2010 end date not specified	Patients attending primary care services in London	40	Primary care units	Administration of rapid point-of-care HIV test
Bassett, D., *et al.* (2012)	**Practical challenges implementing national HIV**	Abstract	Record of HIV test	not reported	July 2011 (two weeks)	Acute medical admissions in central Manchester	1	Acute medical admissions	Record of HIV test administration

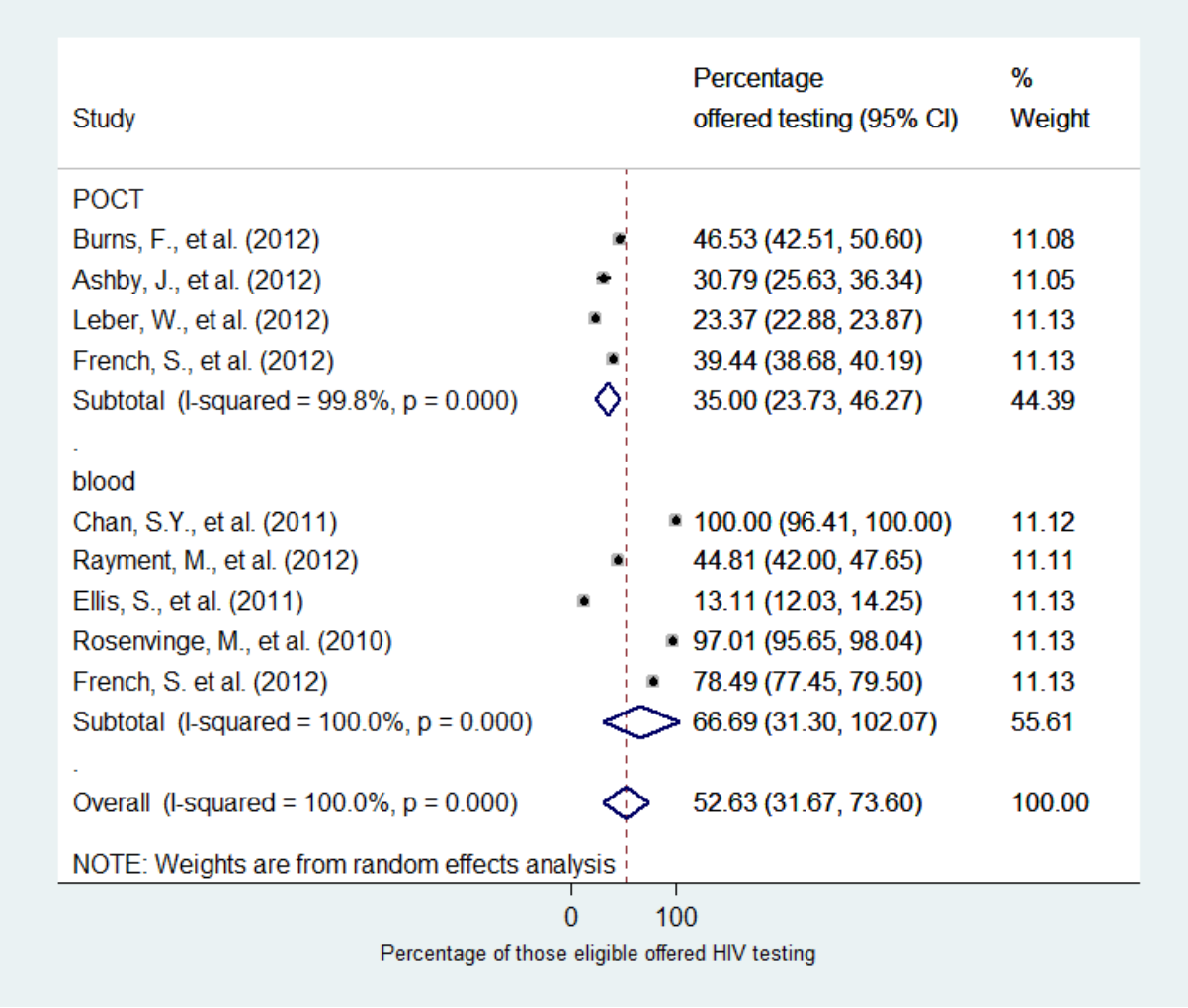
	testing guidelines in general medical admissions								
Rosenvinge, M., *et al.* (2010)	**A successful uptake of HIV testing in south London termination of pregnancy services**	Abstract	Record of consent for an HIV test	Known HIV positive, recent (< 6 months) HIV negative test, repeat attendance	April - December 2009 (9 months)	Women attending termination of pregnancy services in south London	2	Termination of pregnancy clinics	Paper and electronic record of HIV test administration
Garrard, N., *et al.* (2010)	**Opt-out HIV testing pilot in termination of pregnancy services - 11-month service evaluation**	Abstract	HIV test recommendation	not reported	November 2008 - September 2009 (11 months)	Women attending termination of Pregnancy services north London	1	Termination of pregnancy clinic	Documentation of HIV test result

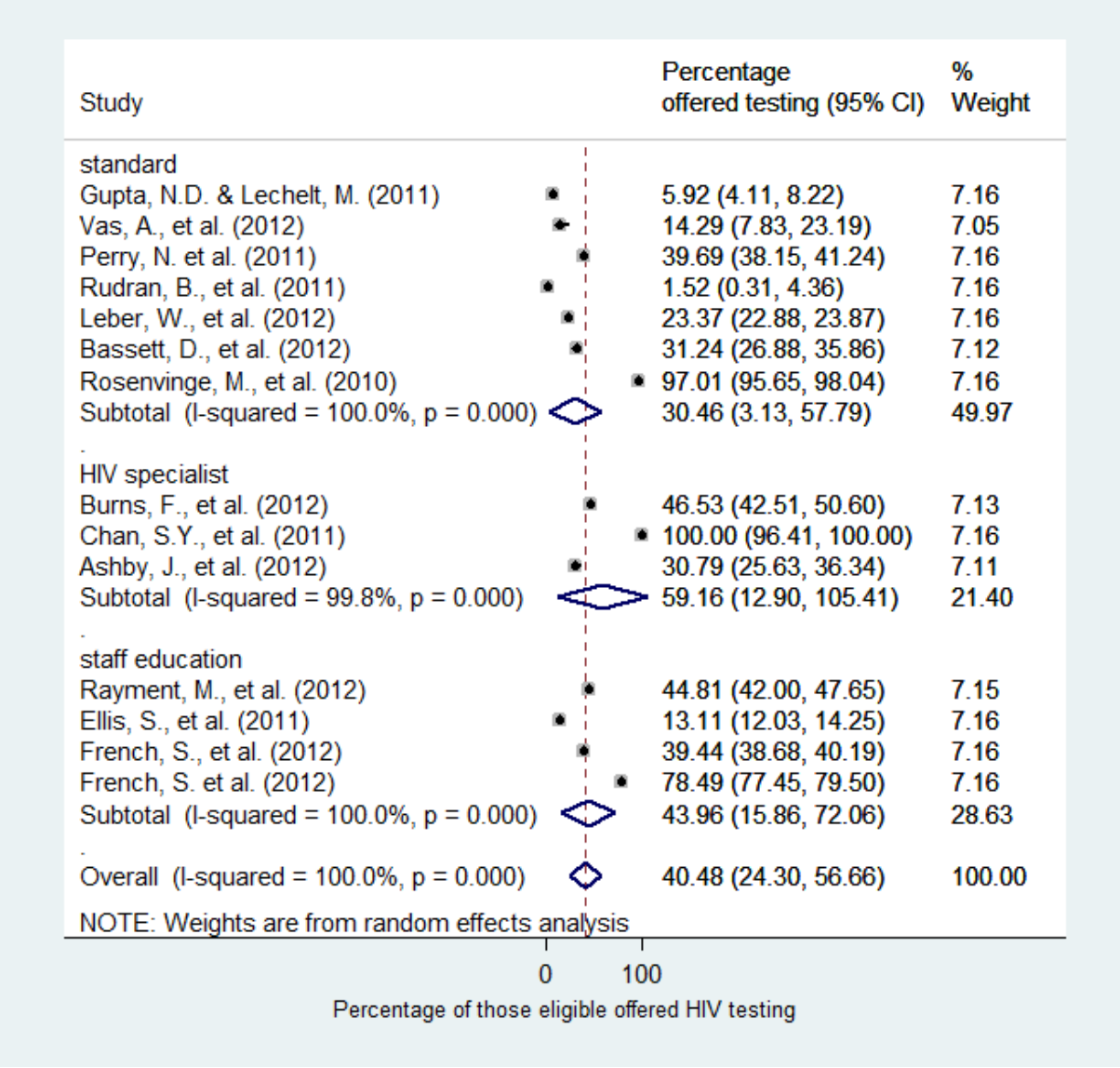
Barbour, A., *et al.* (2011)	**Opt-out HIV testing policy implemented as routine standard of care for acute medical admissions in a high prevalence area**	Abstract	Record of HIV test	<16 and >79 years,	July 2011 – December 2011 (6 months)	Patients attending acute medical admissions in Croydon	1	Acute medical admissions	HIV testing
Rycroft, J., *et al.* (2012)	**HIV testing in the acute medical unit - setting the scene for universal opt-out testing**	Abstract	Laboratory record of HIV test	Not reported	June & November 2011 (audited 2 weeks for each admissions cycle)	Patients attending acute medical admissions in south east London	1	Acute medical admissions	Record of HIV test in laboratory database
Page, I., *et al.* (2011)	**The impact of new national HIV testing guidelines at a district**	Paper	Laboratory record of HIV test	HIV test requests from GUM clinics	October 2008 – September 2009	Inpatients in Blackpool	1	Secondary care hospital	Laboratory record of HIV test

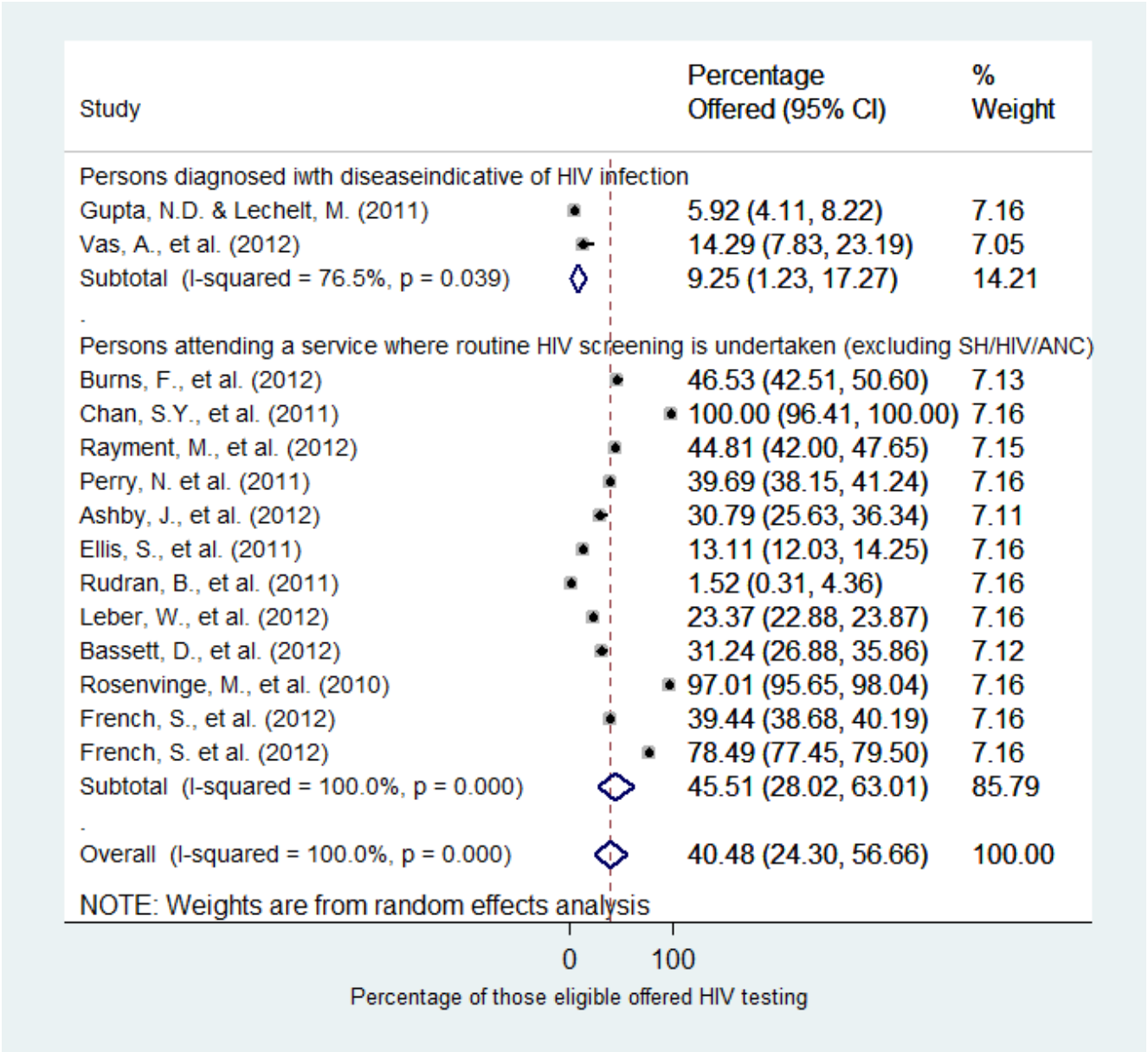
	general hospital in an area of high HIV seroprevalence								
Palfreeman, A., et al. (2013)	HIV testing for acute medical admissions: evaluation of a pilot study in Leicester, England	Paper	Laboratory record of HIV test	Not reported	September 2008 – August 2011 (36 months)	Patients admitted to AMU in Leicester	1	Secondary care hospital	Laboratory record of HIV test

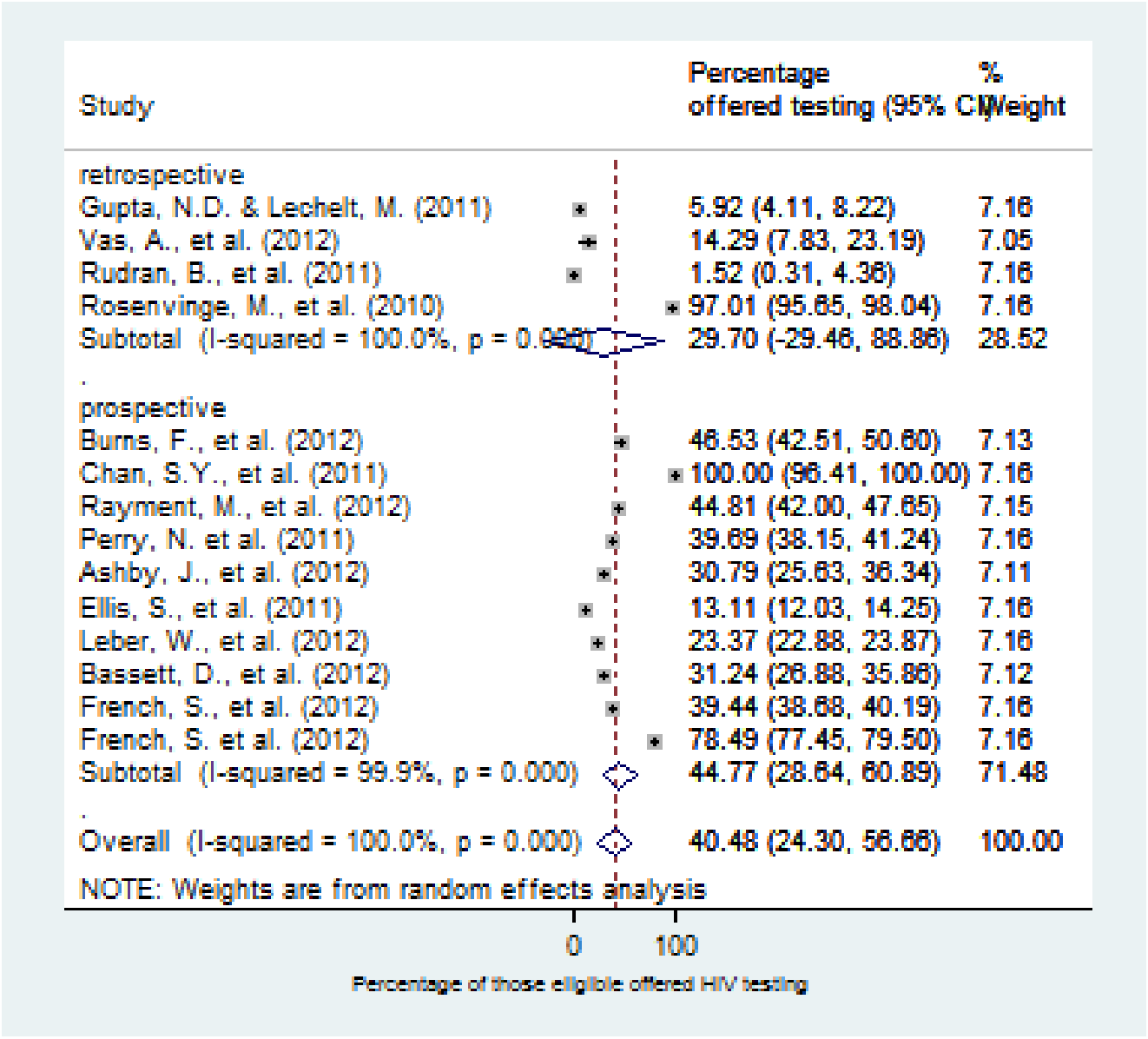
Appendix D: Forest plot for meta-analysis of percentage test offer a) overall and stratified by b) Test Type c) Testing Strategy d) Delivery Model e) Location f) Study Type and g) Patient Group

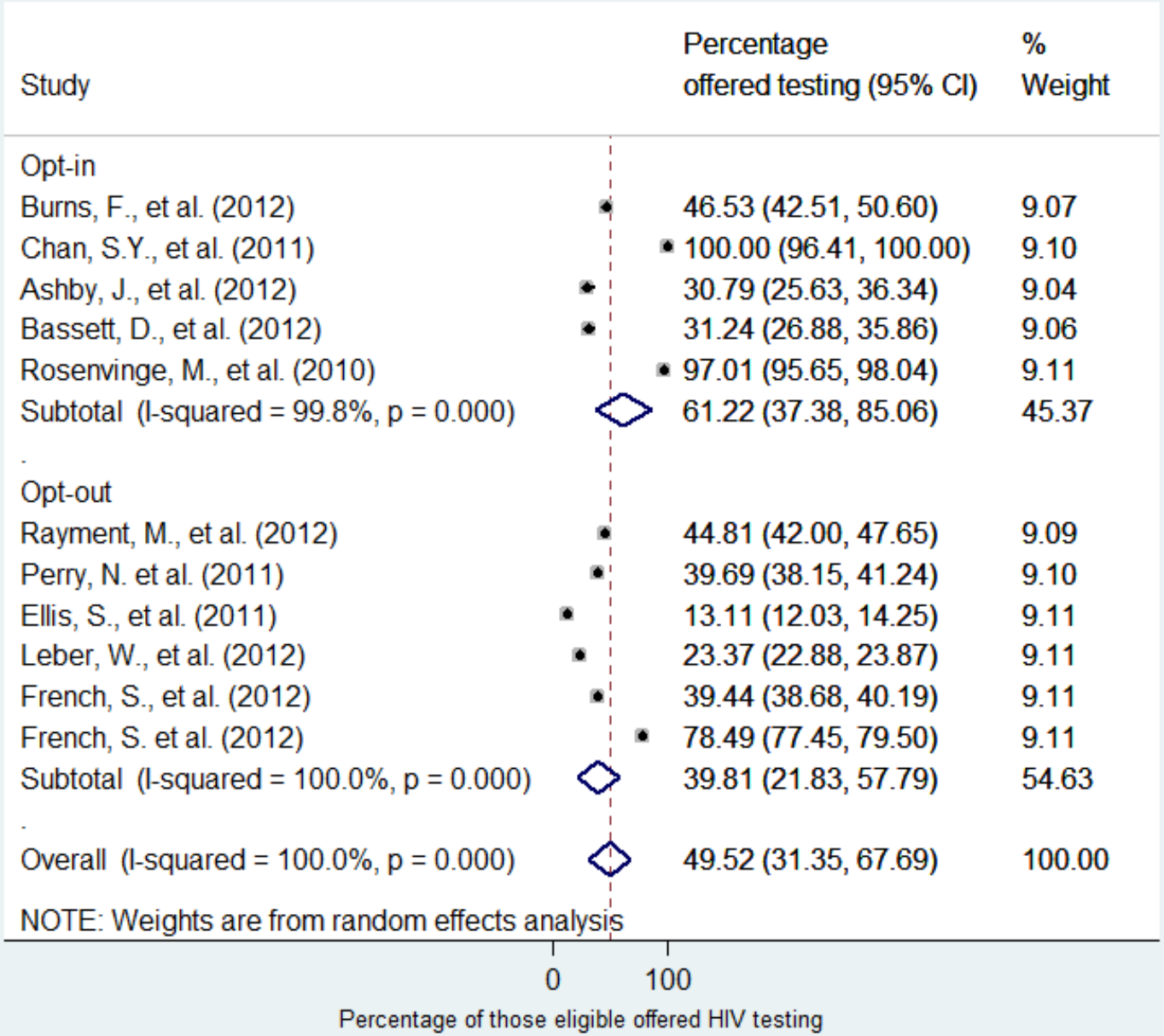


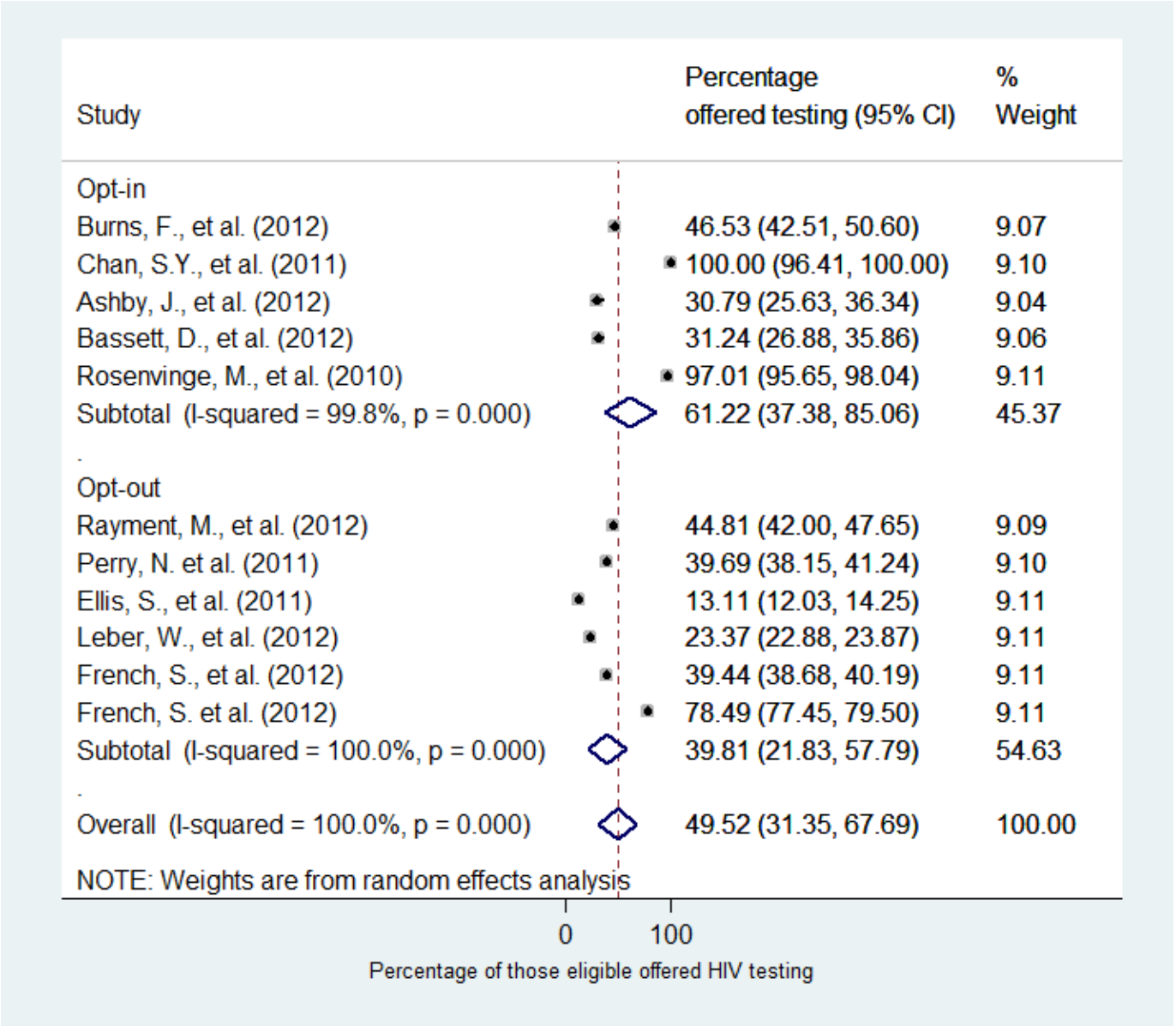

Study
Percentage offered testing (95% CI)
% Weight
POCT
Burns, F., et al. (2012) 46.53 (42.51, 50.60) 11.08
Ashby, J., et al. (2012) 30.79 (25.63, 36.34) 11.05
Leber, W., et al. (2012) 23.37 (22.88, 23.87) 11.13
French, S., et al. (2012) 39.44 (38.68, 40.19) 11.13
Subtotal (I-squared = 99.8%, p = 0.000) 35.00 (23.73, 46.27) 44.39
blood
Chan, S.Y., et al. (2011) 100.00 (96.41, 100.00) 11.12
Rayment, M., et al. (2012) 44.81 (42.00, 47.65) 11.11
Ellis, S., et al. (2011) 13.11 (12.03, 14.25) 11.13
Rosenvinge, M., et al. (2010) 97.01 (95.65, 98.04) 11.13
French, S. et al. (2012) 78.49 (77.45, 79.50) 11.13
Subtotal (I-squared = 100.0%, p = 0.000) 66.69 (31.30, 102.07) 55.61
Overall (I-squared = 100.0%, p = 0.000) 52.63 (31.67, 73.60) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

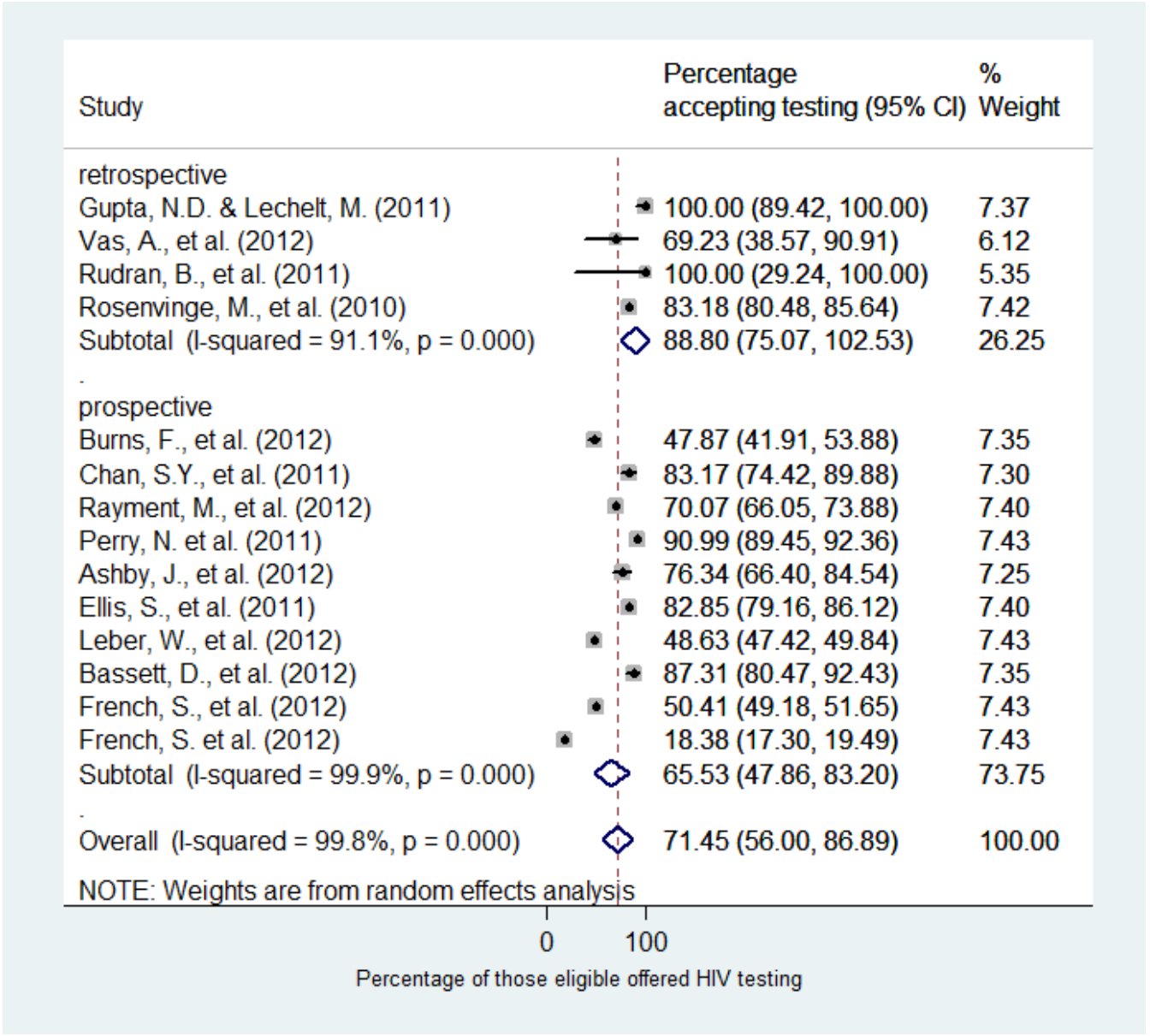

Study
Percentage offered testing (95% CI)
% Weight
standard
Gupta, N.D. & Lechelt, M. (2011) 5.92 (4.11, 8.22) 7.16
Vas, A., et al. (2012) 14.29 (7.83, 23.19) 7.05
Perry, N. et al. (2011) 39.69 (38.15, 41.24) 7.16
Rudran, B., et al. (2011) 1.52 (0.31, 4.36) 7.16
Leber, W., et al. (2012) 23.37 (22.88, 23.87) 7.16
Bassett, D., et al. (2012) 31.24 (26.88, 35.86) 7.12
Rosenvinge, M., et al. (2010) 97.01 (95.65, 98.04) 7.16
Subtotal (I-squared = 100.0%, p = 0.000) 30.46 (3.13, 57.79) 49.97
HIV specialist
Burns, F., et al. (2012) 46.53 (42.51, 50.60) 7.13
Chan, S.Y., et al. (2011) 100.00 (96.41, 100.00) 7.16
Ashby, J., et al. (2012) 30.79 (25.63, 36.34) 7.11
Subtotal (I-squared = 99.8%, p = 0.000) 59.16 (12.90, 105.41) 21.40
staff education
Rayment, M., et al. (2012) 44.81 (42.00, 47.65) 7.15
Ellis, S., et al. (2011) 13.11 (12.03, 14.25) 7.16
French, S., et al. (2012) 39.44 (38.68, 40.19) 7.16
French, S. et al. (2012) 78.49 (77.45, 79.50) 7.16
Subtotal (I-squared = 100.0%, p = 0.000) 43.96 (15.86, 72.06) 28.63
Overall (I-squared = 100.0%, p = 0.000) 40.48 (24.30, 56.66) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

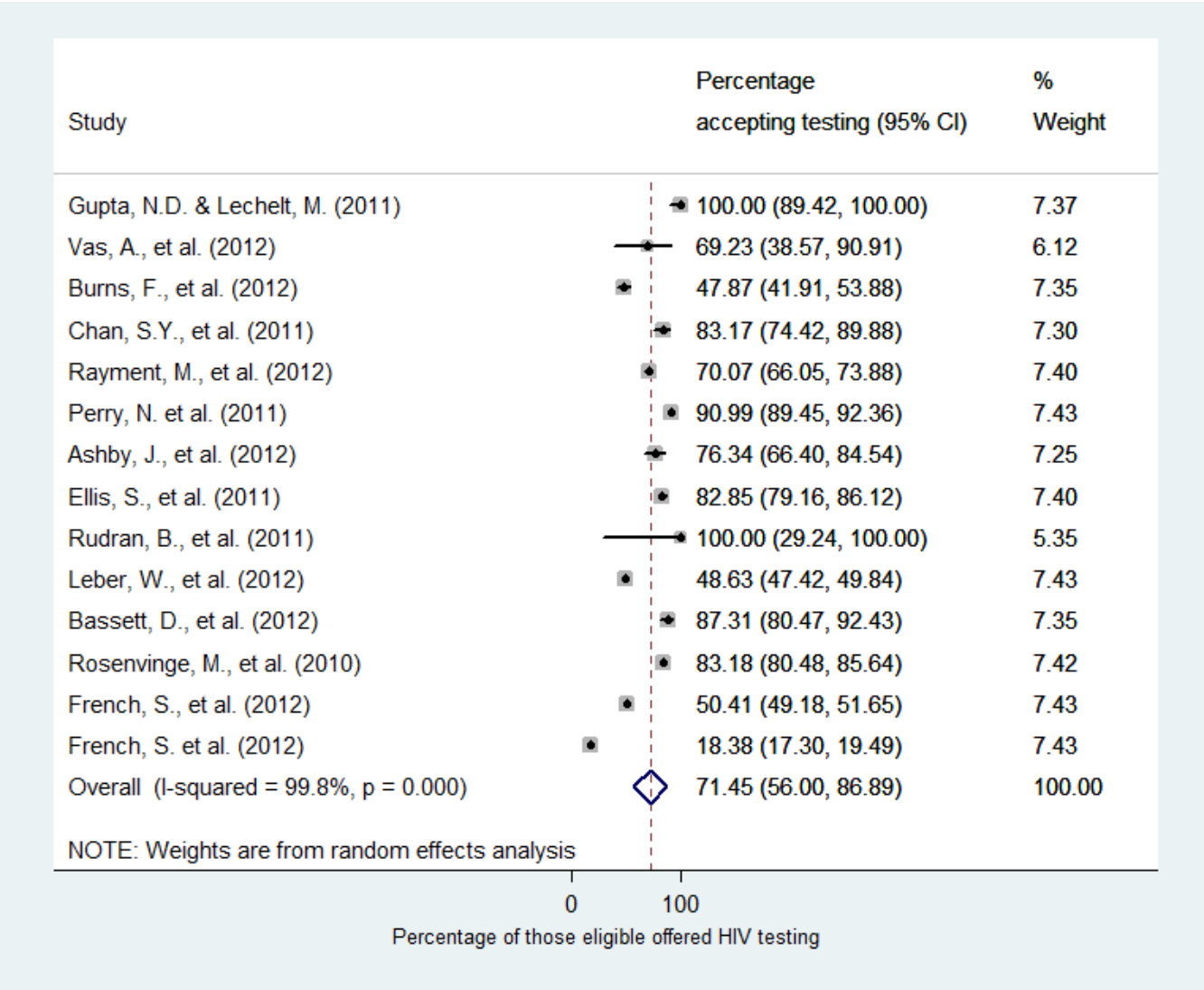

Study
Percentage Offered (95% CI)
% Weight
Persons diagnosed iwth diseaseindicative of HIV infection
Gupta, N.D. & Lechelt, M. (2011) 5.92 (4.11, 8.22) 7.16
Vas, A., et al. (2012) 14.29 (7.83, 23.19) 7.05
Subtotal (I-squared = 76.5%, p = 0.039) 9.25 (1.23, 17.27) 14.21
Persons attending a service where routine HIV screening is undertaken (excluding SH/HIV/ANC)
Burns, F., et al. (2012) 46.53 (42.51, 50.60) 7.13
Chan, S.Y., et al. (2011) 100.00 (96.41, 100.00) 7.16
Rayment, M., et al. (2012) 44.81 (42.00, 47.65) 7.15
Perry, N. et al. (2011) 39.69 (38.15, 41.24) 7.16
Ashby, J., et al. (2012) 30.79 (25.63, 36.34) 7.11
Ellis, S., et al. (2011) 13.11 (12.03, 14.25) 7.16
Rudran, B., et al. (2011) 1.52 (0.31, 4.36) 7.16
Leber, W., et al. (2012) 23.37 (22.88, 23.87) 7.16
Bassett, D., et al. (2012) 31.24 (26.88, 35.86) 7.12
Rosenvinge, M., et al. (2010) 97.01 (95.65, 98.04) 7.16
French, S., et al. (2012) 39.44 (38.68, 40.19) 7.16
French, S. et al. (2012) 78.49 (77.45, 79.50) 7.16
Subtotal (I-squared = 100.0%, p = 0.000) 45.51 (28.02, 63.01) 85.79
Overall (I-squared = 100.0%, p = 0.000) 40.48 (24.30, 56.66) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing


Study
Percentage offered testing (95% CI)
% Weight
retrospective
Gupta, N.D. & Lechelt, M. (2011) 5.92 (4.11, 8.22) 7.16
Vas, A., et al. (2012) 14.29 (7.83, 23.19) 7.05
Rudran, B., et al. (2011) 1.52 (0.31, 4.36) 7.16
Rosenvinge, M., et al. (2010) 97.01 (95.65, 98.04) 7.16
Subtotal (I-squared = 100.0%, p = 0.000) 29.70 (-29.46, 88.86) 28.52
prospective
Burns, F., et al. (2012) 46.53 (42.51, 50.60) 7.13
Chan, S.Y., et al. (2011) 100.00 (96.41, 100.00) 7.16
Rayment, M., et al. (2012) 44.81 (42.00, 47.65) 7.15
Perry, N. et al. (2011) 39.69 (38.15, 41.24) 7.16
Ashby, J., et al. (2012) 30.79 (25.63, 36.34) 7.11
Ellis, S., et al. (2011) 13.11 (12.03, 14.25) 7.16
Leber, W., et al. (2012) 23.37 (22.88, 23.87) 7.16
Bassett, D., et al. (2012) 31.24 (26.88, 35.86) 7.12
French, S., et al. (2012) 39.44 (38.68, 40.19) 7.16
French, S. et al. (2012) 78.49 (77.45, 79.50) 7.16
Subtotal (I-squared = 99.9%, p = 0.000) 44.77 (28.64, 60.89) 71.48
Overall (I-squared = 100.0%, p = 0.000) 40.48 (24.30, 56.66) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

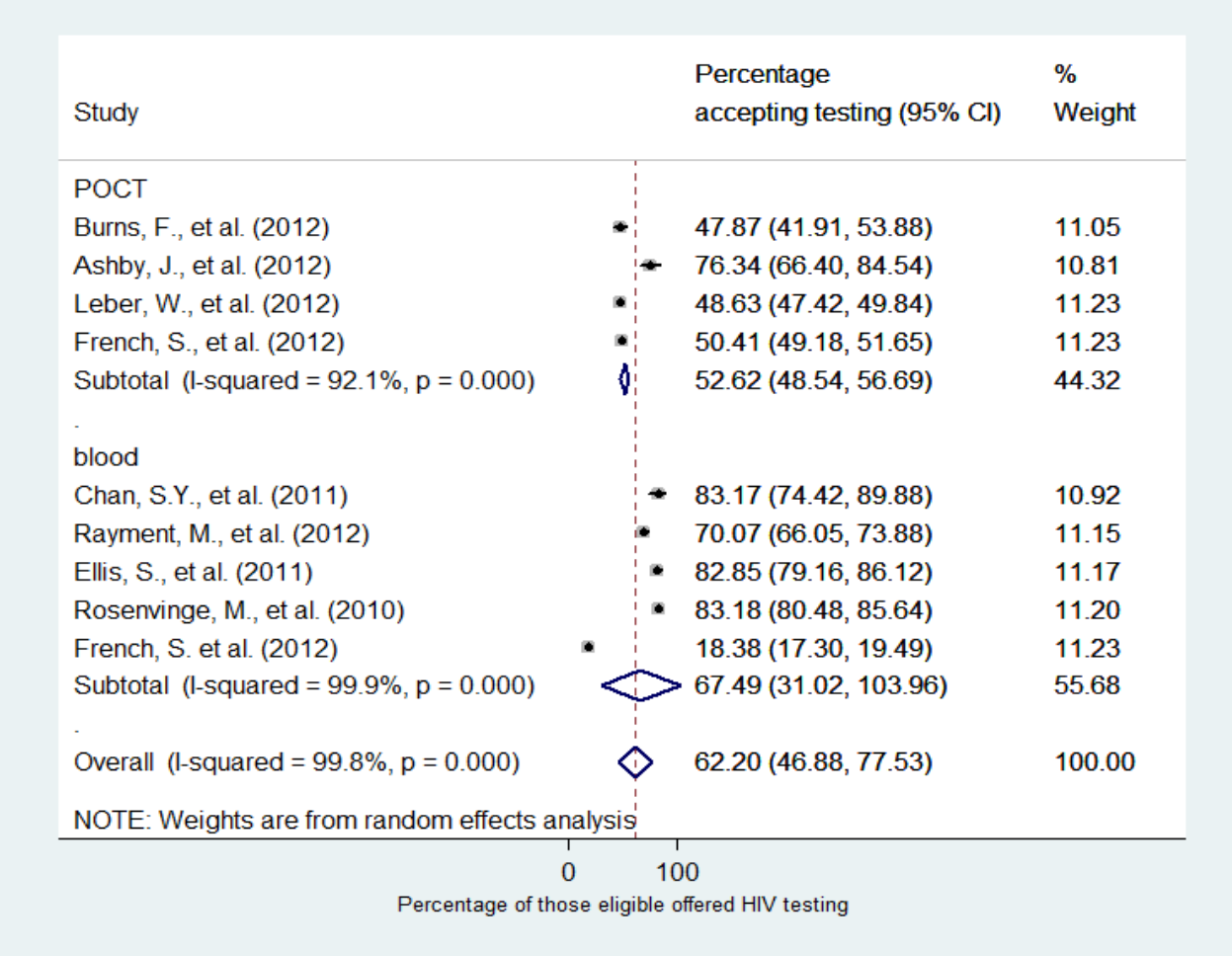

Study
Percentage offered testing (95% CI)
% Weight
Opt-in
Burns, F., et al. (2012) 46.53 (42.51, 50.60) 9.07
Chan, S.Y., et al. (2011) 100.00 (96.41, 100.00) 9.10
Ashby, J., et al. (2012) 30.79 (25.63, 36.34) 9.04
Bassett, D., et al. (2012) 31.24 (26.88, 35.86) 9.06
Rosenvinge, M., et al. (2010) 97.01 (95.65, 98.04) 9.11
Subtotal (I-squared = 99.8%, p = 0.000) 61.22 (37.38, 85.06) 45.37
Opt-out
Rayment, M., et al. (2012) 44.81 (42.00, 47.65) 9.09
Perry, N. et al. (2011) 39.69 (38.15, 41.24) 9.10
Ellis, S., et al. (2011) 13.11 (12.03, 14.25) 9.11
Leber, W., et al. (2012) 23.37 (22.88, 23.87) 9.11
French, S., et al. (2012) 39.44 (38.68, 40.19) 9.11
French, S. et al. (2012) 78.49 (77.45, 79.50) 9.11
Subtotal (I-squared = 100.0%, p = 0.000) 39.81 (21.83, 57.79) 54.63
Overall (I-squared = 100.0%, p = 0.000) 49.52 (31.35, 67.69) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

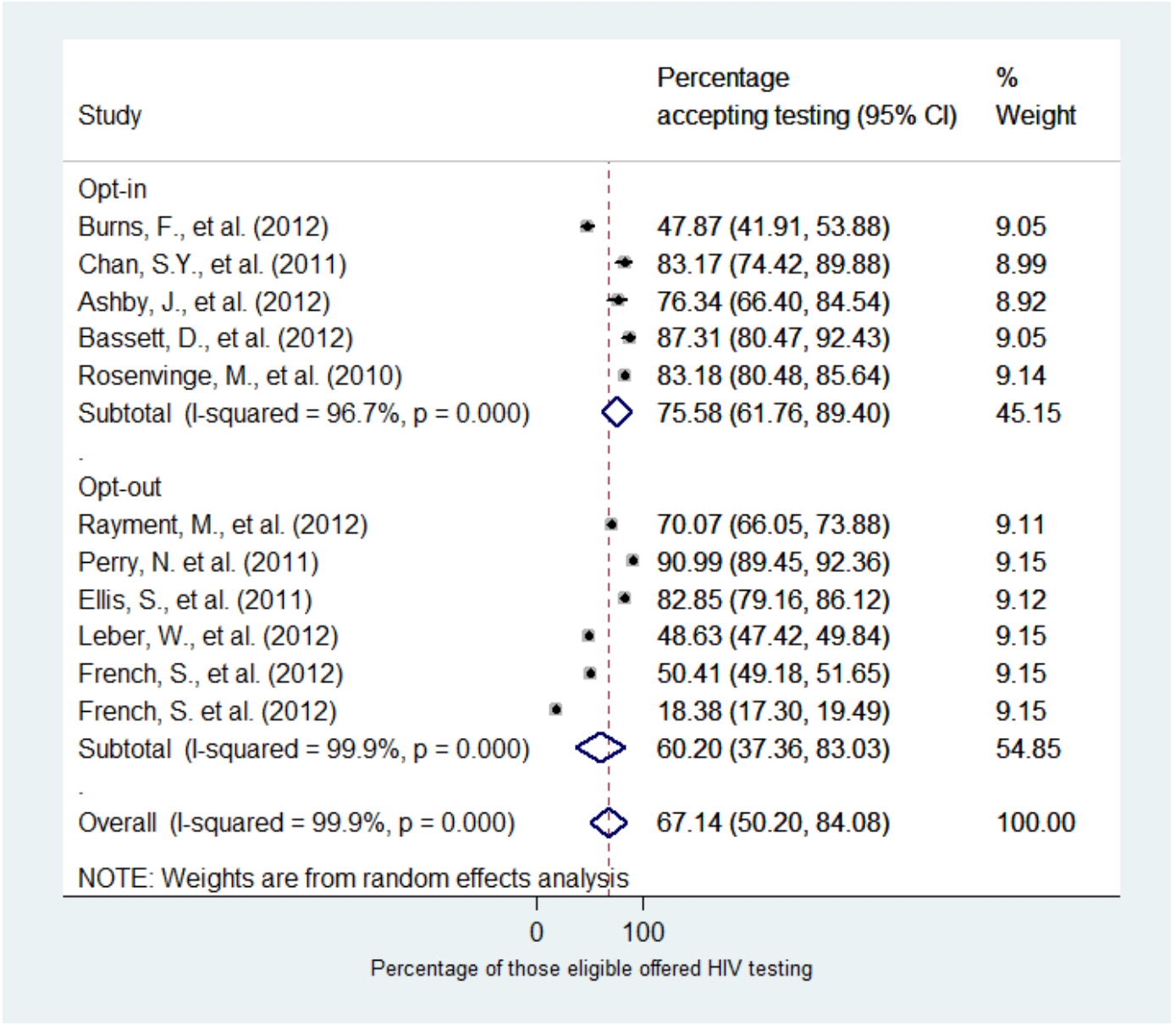

Study
Percentage offered testing (95% CI)
% Weight
Opt-in
Burns, F., et al. (2012) 46.53 (42.51, 50.60) 9.07
Chan, S.Y., et al. (2011) 100.00 (96.41, 100.00) 9.10
Ashby, J., et al. (2012) 30.79 (25.63, 36.34) 9.04
Bassett, D., et al. (2012) 31.24 (26.88, 35.86) 9.06
Rosenvinge, M., et al. (2010) 97.01 (95.65, 98.04) 9.11
Subtotal (I-squared = 99.8%, p = 0.000) 61.22 (37.38, 85.06) 45.37
Opt-out
Rayment, M., et al. (2012) 44.81 (42.00, 47.65) 9.09
Perry, N. et al. (2011) 39.69 (38.15, 41.24) 9.10
Ellis, S., et al. (2011) 13.11 (12.03, 14.25) 9.11
Leber, W., et al. (2012) 23.37 (22.88, 23.87) 9.11
French, S., et al. (2012) 39.44 (38.68, 40.19) 9.11
French, S. et al. (2012) 78.49 (77.45, 79.50) 9.11
Subtotal (I-squared = 100.0%, p = 0.000) 39.81 (21.83, 57.79) 54.63
Overall (I-squared = 100.0%, p = 0.000) 49.52 (31.35, 67.69) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

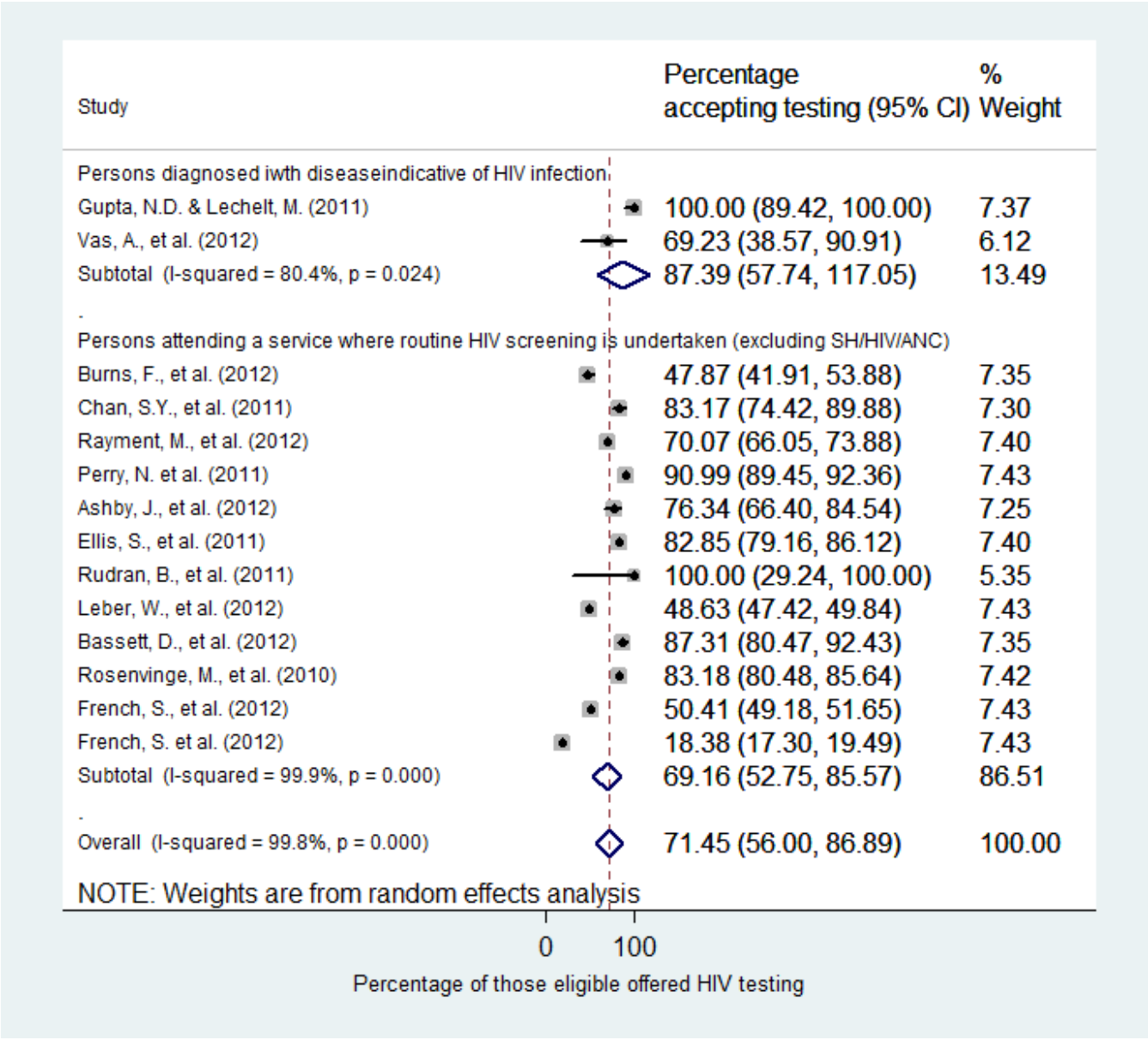

Study
Percentage accepting testing (95% CI)
% Weight
retrospective
Gupta, N.D. & Lechelt, M. (2011) 100.00 (89.42, 100.00) 7.37
Vas, A., et al. (2012) 69.23 (38.57, 90.91) 6.12
Rudran, B., et al. (2011) 100.00 (29.24, 100.00) 5.35
Rosenvinge, M., et al. (2010) 83.18 (80.48, 85.64) 7.42
Subtotal (I-squared = 91.1%, p = 0.000) 88.80 (75.07, 102.53) 26.25
prospective
Burns, F., et al. (2012) 47.87 (41.91, 53.88) 7.35
Chan, S.Y., et al. (2011) 83.17 (74.42, 89.88) 7.30
Rayment, M., et al. (2012) 70.07 (66.05, 73.88) 7.40
Perry, N. et al. (2011) 90.99 (89.45, 92.36) 7.43
Ashby, J., et al. (2012) 76.34 (66.40, 84.54) 7.25
Ellis, S., et al. (2011) 82.85 (79.16, 86.12) 7.40
Leber, W., et al. (2012) 48.63 (47.42, 49.84) 7.43
Bassett, D., et al. (2012) 87.31 (80.47, 92.43) 7.35
French, S., et al. (2012) 50.41 (49.18, 51.65) 7.43
French, S. et al. (2012) 18.38 (17.30, 19.49) 7.43
Subtotal (I-squared = 99.9%, p = 0.000) 65.53 (47.86, 83.20) 73.75
Overall (I-squared = 99.8%, p = 0.000) 71.45 (56.00, 86.89) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

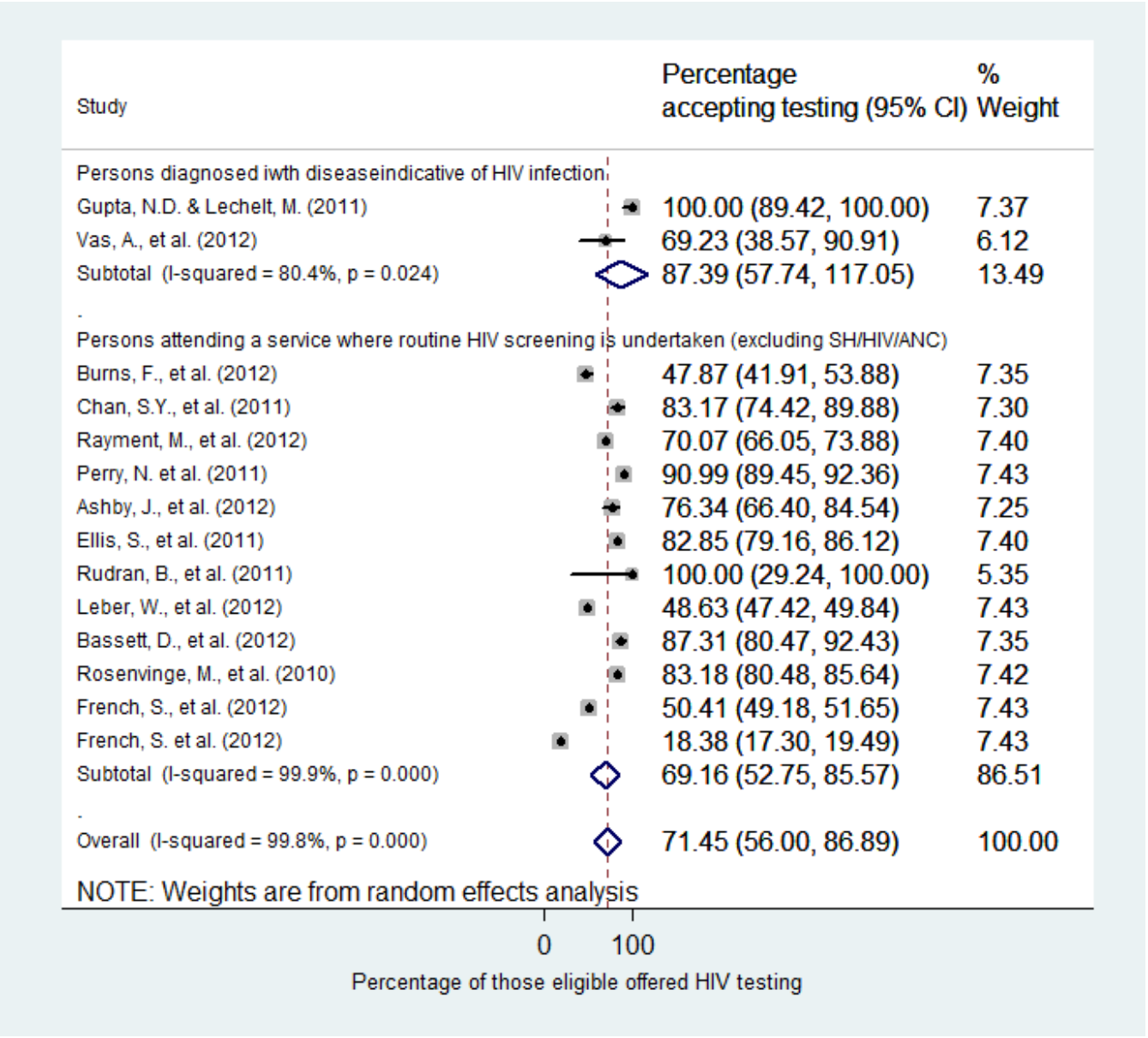

Study
Percentage accepting testing (95% CI)
% Weight
Gupta, N.D. & Lechelt, M. (2011) 100.00 (89.42, 100.00) 7.37
Vas, A., et al. (2012) 69.23 (38.57, 90.91) 6.12
Burns, F., et al. (2012) 47.87 (41.91, 53.88) 7.35
Chan, S.Y., et al. (2011) 83.17 (74.42, 89.88) 7.30
Rayment, M., et al. (2012) 70.07 (66.05, 73.88) 7.40
Perry, N. et al. (2011) 90.99 (89.45, 92.36) 7.43
Ashby, J., et al. (2012) 76.34 (66.40, 84.54) 7.25
Ellis, S., et al. (2011) 82.85 (79.16, 86.12) 7.40
Rudran, B., et al. (2011) 100.00 (29.24, 100.00) 5.35
Leber, W., et al. (2012) 48.63 (47.42, 49.84) 7.43
Bassett, D., et al. (2012) 87.31 (80.47, 92.43) 7.35
Rosenvinge, M., et al. (2010) 83.18 (80.48, 85.64) 7.42
French, S., et al. (2012) 50.41 (49.18, 51.65) 7.43
French, S. et al. (2012) 18.38 (17.30, 19.49) 7.43
Overall (I-squared = 99.8%, p = 0.000) 71.45 (56.00, 86.89) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

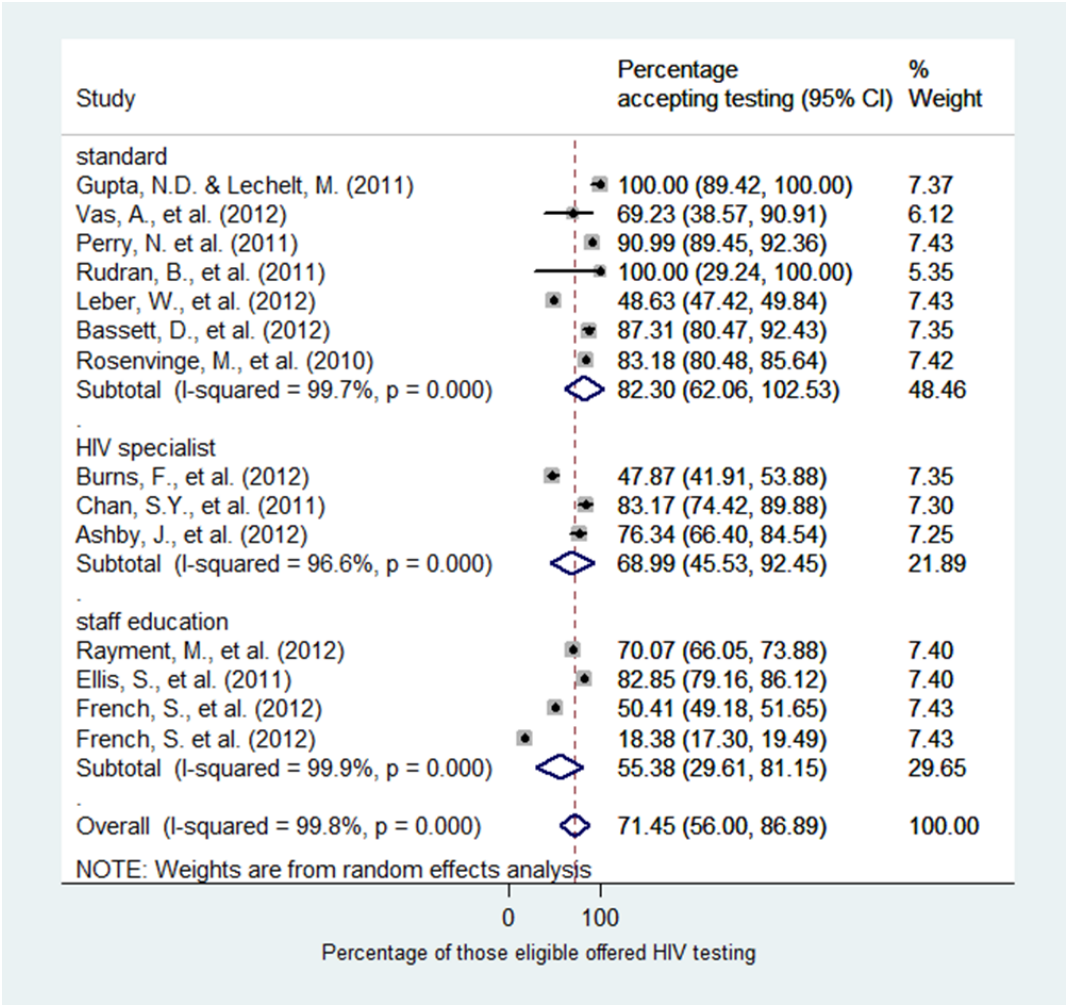
Appendix E: Forest plot for meta-analysis of percentage test acceptance a) overall and stratified by b) Test Type b) Testing Strategy c) Delivery Model e) Location f) Study Type and g) Patient Group



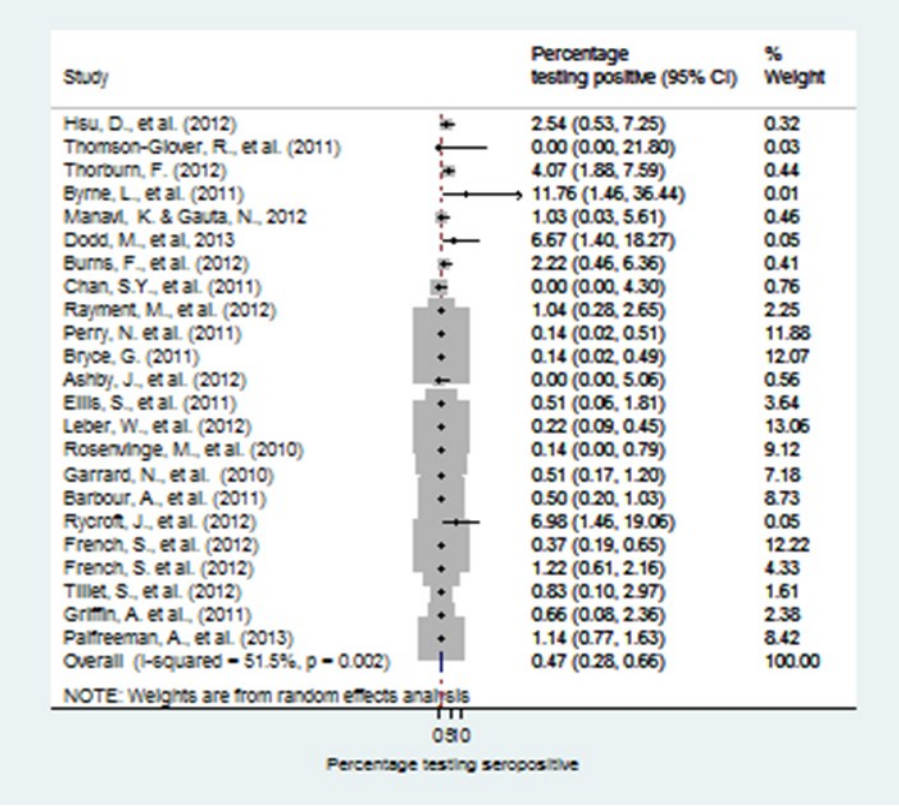

Study
Percentage accepting testing (95% CI)
% Weight
Opt-in
Burns, F., et al. (2012) 47.87 (41.91, 53.88) 9.05
Chan, S.Y., et al. (2011) 83.17 (74.42, 89.88) 8.99
Ashby, J., et al. (2012) 76.34 (66.40, 84.54) 8.92
Bassett, D., et al. (2012) 87.31 (80.47, 92.43) 9.05
Rosenvinge, M., et al. (2010) 83.18 (80.48, 85.64) 9.14
Subtotal (I-squared = 96.7%, p = 0.000) 75.58 (61.76, 89.40) 45.15
Opt-out
Rayment, M., et al. (2012) 70.07 (66.05, 73.88) 9.11
Perry, N. et al. (2011) 90.99 (89.45, 92.36) 9.15
Ellis, S., et al. (2011) 82.85 (79.16, 86.12) 9.12
Leber, W., et al. (2012) 48.63 (47.42, 49.84) 9.15
French, S., et al. (2012) 50.41 (49.18, 51.65) 9.15
French, S. et al. (2012) 18.38 (17.30, 19.49) 9.15
Subtotal (I-squared = 99.9%, p = 0.000) 60.20 (37.36, 83.03) 54.85
Overall (I-squared = 99.9%, p = 0.000) 67.14 (50.20, 84.08) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

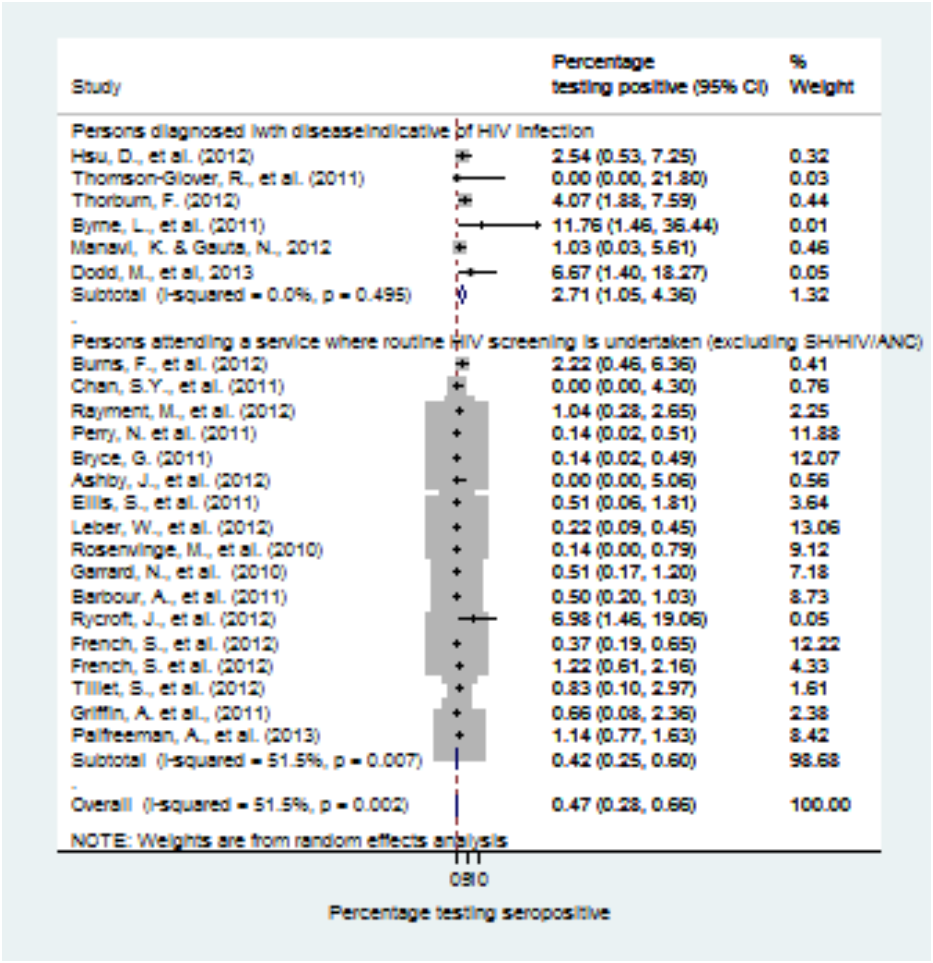

Study
Percentage accepting testing (95% CI)
% Weight
Persons diagnosed iwth diseaseindicative of HIV infection
Gupta, N.D. & Lechelt, M. (2011) 100.00 (89.42, 100.00) 7.37
Vas, A., et al. (2012) 69.23 (38.57, 90.91) 6.12
Subtotal (I-squared = 80.4%, p = 0.024) 87.39 (57.74, 117.05) 13.49
Persons attending a service where routine HIV screening is undertaken (excluding SH/HIV/ANC)
Burns, F., et al. (2012) 47.87 (41.91, 53.88) 7.35
Chan, S.Y., et al. (2011) 83.17 (74.42, 89.88) 7.30
Rayment, M., et al. (2012) 70.07 (66.05, 73.88) 7.40
Perry, N. et al. (2011) 90.99 (89.45, 92.36) 7.43
Ashby, J., et al. (2012) 76.34 (66.40, 84.54) 7.25
Ellis, S., et al. (2011) 82.85 (79.16, 86.12) 7.40
Rudran, B., et al. (2011) 100.00 (29.24, 100.00) 5.35
Leber, W., et al. (2012) 48.63 (47.42, 49.84) 7.43
Bassett, D., et al. (2012) 87.31 (80.47, 92.43) 7.35
Rosenvinge, M., et al. (2010) 83.18 (80.48, 85.64) 7.42
French, S., et al. (2012) 50.41 (49.18, 51.65) 7.43
French, S. et al. (2012) 18.38 (17.30, 19.49) 7.43
Subtotal (I-squared = 99.9%, p = 0.000) 69.16 (52.75, 85.57) 86.51
Overall (I-squared = 99.8%, p = 0.000) 71.45 (56.00, 86.89) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

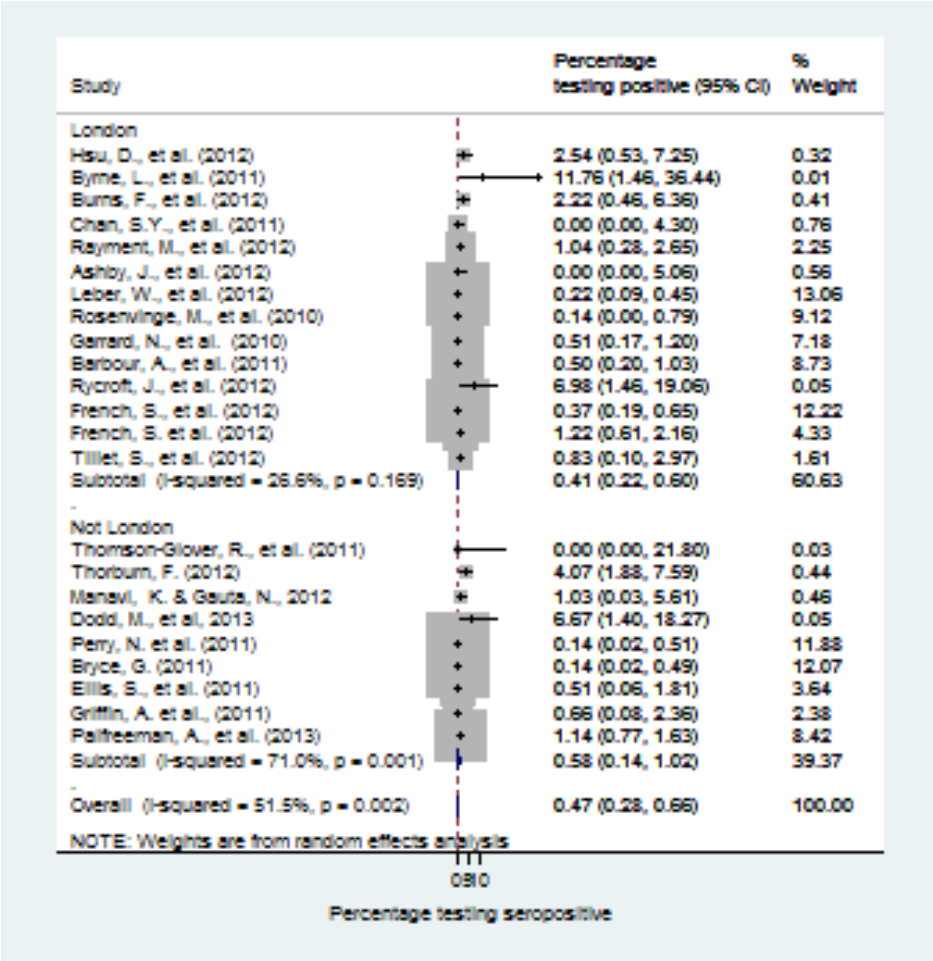

Study
Percentage accepting testing (95% CI)
% Weight
Persons diagnosed iwth diseaseindicative of HIV infection
Gupta, N.D. & Lechelt, M. (2011) 100.00 (89.42, 100.00) 7.37
Vas, A., et al. (2012) 69.23 (38.57, 90.91) 6.12
Subtotal (I-squared = 80.4%, p = 0.024) 87.39 (57.74, 117.05) 13.49
Persons attending a service where routine HIV screening is undertaken (excluding SH/HIV/ANC)
Burns, F., et al. (2012) 47.87 (41.91, 53.88) 7.35
Chan, S.Y., et al. (2011) 83.17 (74.42, 89.88) 7.30
Rayment, M., et al. (2012) 70.07 (66.05, 73.88) 7.40
Perry, N. et al. (2011) 90.99 (89.45, 92.36) 7.43
Ashby, J., et al. (2012) 76.34 (66.40, 84.54) 7.25
Ellis, S., et al. (2011) 82.85 (79.16, 86.12) 7.40
Rudran, B., et al. (2011) 100.00 (29.24, 100.00) 5.35
Leber, W., et al. (2012) 48.63 (47.42, 49.84) 7.43
Bassett, D., et al. (2012) 87.31 (80.47, 92.43) 7.35
Rosenvinge, M., et al. (2010) 83.18 (80.48, 85.64) 7.42
French, S., et al. (2012) 50.41 (49.18, 51.65) 7.43
French, S. et al. (2012) 18.38 (17.30, 19.49) 7.43
Subtotal (I-squared = 99.9%, p = 0.000) 69.16 (52.75, 85.57) 86.51
Overall (I-squared = 99.8%, p = 0.000) 71.45 (56.00, 86.89) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing


Study
Percentage accepting testing (95% CI)
% Weight
standard
Gupta, N.D. & Lechelt, M. (2011) 100.00 (89.42, 100.00) 7.37
Vas, A., et al. (2012) 69.23 (38.57, 90.91) 6.12
Perry, N. et al. (2011) 90.99 (89.45, 92.36) 7.43
Rudran, B., et al. (2011) 100.00 (29.24, 100.00) 5.35
Leber, W., et al. (2012) 48.63 (47.42, 49.84) 7.43
Bassett, D., et al. (2012) 87.31 (80.47, 92.43) 7.35
Rosenvinge, M., et al. (2010) 83.18 (80.48, 85.64) 7.42
Subtotal (I-squared = 99.7%, p = 0.000) 82.30 (62.06, 102.53) 48.46
HIV specialist
Burns, F., et al. (2012) 47.87 (41.91, 53.88) 7.35
Chan, S.Y., et al. (2011) 83.17 (74.42, 89.88) 7.30
Ashby, J., et al. (2012) 76.34 (66.40, 84.54) 7.25
Subtotal (I-squared = 96.6%, p = 0.000) 68.99 (45.53, 92.45) 21.89
staff education
Rayment, M., et al. (2012) 70.07 (66.05, 73.88) 7.40
Ellis, S., et al. (2011) 82.85 (79.16, 86.12) 7.40
French, S., et al. (2012) 50.41 (49.18, 51.65) 7.43
French, S. et al. (2012) 18.38 (17.30, 19.49) 7.43
Subtotal (I-squared = 99.9%, p = 0.000) 55.38 (29.61, 81.15) 29.65
Overall (I-squared = 99.8%, p = 0.000) 71.45 (56.00, 86.89) 100.00
NOTE: Weights are from random effects analysis
0
100
Percentage of those eligible offered HIV testing

Appendix F: Forest plot for meta- Appendix F: Forest plot for meta-analysis of percentage testing positive for HIV a) overall and stratified by b) Location c) Patient Group




Study
Percentage testing positive (95% CI)
% Weight
Persons diagnosed iwth diseaseindicative of HIV infection
Hsu, D., et al. (2012) 2.54 (0.53, 7.25) 0.32
Thomson-Glover, R., et al. (2011) 0.00 (0.00, 21.80) 0.03
Thorburn, F. (2012) 4.07 (1.88, 7.59) 0.44
Byrne, L., et al. (2011) 11.76 (1.46, 36.44) 0.01
Manavi, K. & Gauta, N., 2012 1.03 (0.03, 5.61) 0.46
Dodd, M., et al, 2013 6.67 (1.40, 18.27) 0.05
Subtotal (I-squared = 0.0%, p = 0.495) 2.71 (1.05, 4.36) 1.32
Persons attending a service where routine HIV screening is undertaken (excluding SH/HIV/ANC)
Burns, F., et al. (2012) 2.22 (0.46, 6.36) 0.41
Chan, S.Y., et al. (2011) 0.00 (0.00, 4.30) 0.76
Rayment, M., et al. (2012) 1.04 (0.28, 2.65) 2.25
Perry, N. et al. (2011) 0.14 (0.02, 0.51) 11.88
Bryce, G. (2011) 0.14 (0.02, 0.49) 12.07
Ashby, J., et al. (2012) 0.00 (0.00, 5.06) 0.56
Ellis, S., et al. (2011) 0.51 (0.06, 1.81) 3.64
Leber, W., et al. (2012) 0.22 (0.09, 0.45) 13.06
Rosenvinge, M., et al. (2010) 0.14 (0.00, 0.79) 9.12
Garrard, N., et al. (2010) 0.51 (0.17, 1.20) 7.18
Barbour, A., et al. (2011) 0.50 (0.20, 1.03) 8.73
Rycroft, J., et al. (2012) 6.98 (1.46, 19.06) 0.05
French, S., et al. (2012) 0.37 (0.19, 0.65) 12.22
French, S. et al. (2012) 1.22 (0.61, 2.16) 4.33
Tillet, S., et al. (2012) 0.83 (0.10, 2.97) 1.61
Griffin, A. et al., (2011) 0.66 (0.08, 2.36) 2.38
Palfreeman, A., et al. (2013) 1.14 (0.77, 1.63) 8.42
Subtotal (I-squared = 51.5%, p = 0.007) 0.42 (0.25, 0.60) 98.68
Overall (I-squared = 51.5%, p = 0.002) 0.47 (0.28, 0.66) 100.00
NOTE: Weights are from random effects analysis
0 5 10
Percentage testing seropositive


Study
Percentage testing positive (95% CI)
% Weight
London
Hsu, D., et al. (2012) 2.54 (0.53, 7.25) 0.32
Byrne, L., et al. (2011) 11.76 (1.46, 36.44) 0.01
Burns, F., et al. (2012) 2.22 (0.46, 6.36) 0.41
Chan, S.Y., et al. (2011) 0.00 (0.00, 4.30) 0.76
Rayment, M., et al. (2012) 1.04 (0.28, 2.65) 2.25
Ashby, J., et al. (2012) 0.00 (0.00, 5.06) 0.56
Leber, W., et al. (2012) 0.22 (0.09, 0.45) 13.06
Rosenvinge, M., et al. (2010) 0.14 (0.00, 0.79) 9.12
Garrard, N., et al. (2010) 0.51 (0.17, 1.20) 7.18
Barbour, A., et al. (2011) 0.50 (0.20, 1.03) 8.73
Rycroft, J., et al. (2012) 6.98 (1.46, 19.06) 0.05
French, S., et al. (2012) 0.37 (0.19, 0.65) 12.22
French, S. et al. (2012) 1.22 (0.61, 2.16) 4.33
Tillet, S., et al. (2012) 0.83 (0.10, 2.97) 1.61
Subtotal (I-squared = 26.6%, p = 0.169) 0.41 (0.22, 0.60) 60.63
Not London
Thomson-Glover, R., et al. (2011) 0.00 (0.00, 21.80) 0.03
Thorburn, F. (2012) 4.07 (1.88, 7.59) 0.44
Manavi, K. & Gaiuta, N., 2012 1.03 (0.03, 5.61) 0.46
Dodd, M., et al, 2013 6.67 (1.40, 18.27) 0.05
Perry, N. et al. (2011) 0.14 (0.02, 0.51) 11.88
Bryce, G. (2011) 0.14 (0.02, 0.49) 12.07
Ellis, S., et al. (2011) 0.51 (0.06, 1.81) 3.64
Griffin, A. et al., (2011) 0.66 (0.08, 2.36) 2.38
Palfreeman, A., et al. (2013) 1.14 (0.77, 1.63) 8.42
Subtotal (I-squared = 71.0%, p = 0.001) 0.58 (0.14, 1.02) 39.37
Overall (I-squared = 51.5%, p = 0.002) 0.47 (0.28, 0.66) 100.00
NOTE: Weights are from random effects analysis
0 5 10
Percentage testing seropositive

Appendix G: Primary variable codes generated – Microsoft Excel 2010

Variable	Parameter	Outcome options	Code
Number	Patient record number database record – anonymised)	Unique	
dob	Reported date of birth	date	
sex	Sex of patient	1. Female 2. Male	
datedx	Date on which the HIV test was taken	date	
cd4	1st recorded cd4+ cell count after diagnosis	Discrete	
ethnicity	Ethnic group and nationality	1. Black African 2. Black Caribbean 3. Black British 4. Black Other 5. Asian 6. Asian British 7. Asian Other 8. White British 9. White Other 10. Mixed 11. Other/Unknown	1. 0 2. 1 3. 2 4. 3 5. 4 6. 5 7. 6 8. 7 9. 8 10. 9 11. 10
sexual	Sexual orientation	1. Homosexual 2. Bisexual	1. 0 2. 1

		3. Heterosexual 4. Unknown	3. 2 4. 3
site	Site from which the newly diagnosed patient was referred from	1. GUM/STI clinic 2. Antenatal care clinic 3. Accident and Emergency 4. Hospital inpatient department 5. General practice 6. Other	1. 0 2. 1 3. 2 4. 3 5. 4 6. 5

Appendix H: New variable codes in data analysis – STATA/SE 12.0

Variable	Parameter	Outcome options	Code
earlylate	Stage of presentation as defined by CD4 cell count	1. Early (≥350 cells/mm^3) 2. Late (<350 cells/mm^3)	1. 1 2. 0
riskearlylate	Stage of presentation as defined by CD4 cell count	1. Late (<350 cells/mm^3) 2. Early (≥350 cells/mm^3)	1. 1 2. 0
latevlate	Stage of presentation as defined by CD4 cell count	1. Early (≥350 cells/mm^3) 2. Late (<350 ≥200 cells/mm^3) 3. Very late (<200 cells/mm^3)	3. 2 4. 1 5. 0
agedays	Age of patient at the time of diagnosis in days	Continuous	
age	Age of patient at the time of diagnosis in years	Continuous	
agecat	Age group (PHE HIV in the UK	1. 15-24 2. 25-39 3. 40-49	1. 0 2. 1 3. 2

	report category)	4. 50+	4. 3
ethgroup	ethnic group of patient	1. Black 2. Asian 3. White 4. Other	1. 0 2. 1 3. 2 4. 3
ethnicity		1. Black African 2. Black Caribbean 3. Black other 4. Asian 5. White 6. Other	1. 0 2. 1 3. 2 4. 3 5. 4 6. 5
sexrisk	Risk of HIV as defined by sexual risk	1. MSM 2. Heterosexual man 3. Heterosexual woman 4. Unknown	1. 0 2. 1 3. 2 4. 3
site	Site from which the newly diagnosed patient was referred from	1. GUM/SH clinic 2. ANC clinic 3. Accident and Emergency 4. Hospital inpatient department/hospital out-patient department 5. General practice 6. Other	1. 0 2. 1 3. 2 4. 3 5. 4 6. 5
setting	Being diagnosed in routine or	1. non-routine 2. routine	1. 0 2. 1

	non-routine setting		

Appendix I: Complete STATA command code for analysis

```
import excel "C:\Users\Rahma Elmahdi\Desktop\newdxanaly2014.xlsx", sheet("Sheet1") firstrow

d

sort cd4

gen agedays = datedx-dob

gen age = agedays/365.2

sum age, d

drop if age <0

sum age, d

sum cd4, d

gen earlylate = 1 if cd4 <1600

drop if earlylate != 1

replace earlylate = 0 if cd4 <350

replace earlylate = 1 if earlylate >=350

tab earlylate

lab define earlylate 0"late(CD4+count<350cell/mm3)" 1"early(CD4+count>=350cells/mm3)"

lab values earlylate earlylate

tab earlylate

lab define sex 0"female" 1"male"

lab values sex sex

tab sex
```

```
gen agecat = age

replace agecat = 0 if agecat >=50

replace agecat = 1 if age <50

replace agecat = 2 if age <40

replace agecat = 3 if age <25

lab define agecat 0">=50" 1"40-49" 2"25-39" 3"15-24"

lab values agecat agecat

tab agecat

gen latevlate = cd4

replace latevlate = 2 if cd4 >=350

replace latevlate = 1 if cd4 <350

replace latevlate = 0 if cd4 <200

tab latevlate

lab define latevlate 0"verylate(CD4count<200cell/mm3)" 1"early(CD4count200-349cells/mm3)"
2"early(CD4count>=350cells/mm3)"

lab values latevlate latevlate

tab latevlate

tab ethnicity

lab define ethnicity 0"black african" 1"black caribbean" 2"black other" 3"asian" 4"white" 5"other"

lab values ethnicity ethnicity

tab ethnicity
```

```
gen ethcat = 0

replace ethcat = 1 if ethnicity == 3

replace ethcat = 2 if ethnicity ==4

replace ethcat = 3 if ethnicity ==5

tab ethcat

lab define ethcat 0"black" 1"asian" 2"white" 3"other"

lab values ethcat ethcat

tab ethcat

tab sexual

lab define sexual 0"homosexual" 1"bisexual" 2"heterosexual" 3"unknown"

lab values sexual sexual

tab sexual sex

gen sexrisk = 0

replace sexrisk = 2 if sexual ==2

replace sexrisk = 1 if sex == 0

replace sexrisk = 3 if sexual ==3

tab sexrisk

lab define sexrisk 0"MSM" 1"heterosexual woman" 2"heterosexual man" 3"unknown"

lab values sexrisk sexrisk

tab sexrisk

lab define site 0"GUM/SH clinic" 1"ANC clinic" 2"A&E" 3"inpatient/outpatient" 4"GP" 5"other"
```

```
lab values site site

tab site

gen setting = site

replace setting = 0 if site <2

replace setting = 1 if site >1

lab define setting 0"routine" 1"non-routine"

lab values setting setting

tab setting

sum cd4, d

sum cd4 if earlylate == 0, d

sum cd4 if earlylate == 1, d

tab sex

tab earlylate if sex == 0

tab ethcat earlylate

tab earlylate if ethcat == 0

tab ethcat

tab sex

tab earlylate if ethcat == 1

tab earlylate if ethcat == 2

tab earlylate if ethcat == 3

sum age, d
```

```
sum age if earlylate == 0, d

sum age if earlylate == 1, d

tab agecat

tab earlylate if agecat == 0

tab earlylate if agecat == 1

tab earlylate if agecat == 2

tab earlylate if agecat == 3

tab sexrisk year if earlylate == 0

tab sexrisk year

tab earlylate sexrisk

tab site earlylate

tab sexual if sex ==1

tab sexrisk if sex ==1

tab sexrisk

tab earlylate year, chi2

tab sexrisk earlylate if sexrisk !=0, chi2

xi: logit earlylate i.sex, or

xi: logit earlylate i.agecat, or

xi: logit earlylate i.ethcat, or

xi: logit earlylate i.sex, or

xi: logit earlylate i.agecat, or
```

```
xi: logit earlylate i.ethcat, or

gen riskearlylate = earlylate

replace riskearlylate = 2 if earlylate == 1

replace riskearlylate = 1 if earlylate == 0

tab riskearlylate

replace riskearlylate = 0 if riskearlylate == 1

replace riskearlylate = 1 if riskearlylate == 2

tab riskearlylate

replace riskearlylate = 0 if earlylate ==1

replace riskearlylate = 1 if earlylate == 0

xi: logistic riskearlylate i.sex, or

xi: logistic riskearlylate i.ethcat, or

xi: logistic riskearlylate i.ethnicity, or

xi: logistic riskearlylate i.sexrisk, or

xi: logistic riskearlylate i.agecat, or

xi: logistic earlylate i.sex, or

xi: logistic earlylate i.ethcat, or

xi: logistic earlylate i.ethnicity, or

xi: logistic earlylate i.sexrisk, or

xi: logistic earlylate i.site, or

xi: logistic earlylate i.setting, or
```

```
xi: logistic riskearlylate i.setting, or

xi: logistic riskearlylate i.setting, or

xi: logistic riskearlylate i.sex i.agecat i.ethcat, or

xi: logistic riskearlylate i.agecat i.sex i.sexrisk i.ethcat, or

xi: logistic riskearlylate i.ethcat i.sex i.sexrisk i.agecat, or

xi: logistic riskearlylate i.sexrisk i.agecat i.ethcat, or

xi: logistic riskearlylate i.setting i.sex i.sexrisk i.ethcat i.agecat, or

xi: logistic earlylate i.sex, or

xi: logistic i.ethnicity i.sex i.sexrisk i.agecat, or

tab ethnicity

xi: logistic earlylate i.ethnicity i.sex i.sexrisk i.agecat, or

xi: logistic riskearlylate i.ethnicity, or

xi: logistic riskearlylate i.ethcat, or

xi: logistic riskearlylate i.ethcat i.sex i.sexrisk i.agecat, or

xi: logistic riskearlylate i.ethnicity i.sex i.sexrisk i.agecat, or

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Appendix J: Missed HIV Study Protocol

Study Title: Missed HIV Study: Missed Testing for HIV

Missed opportunities for testing and factors contributing to late presentation of HIV in North West London

Ethics Ref: 12/LO/0779

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Collaborators:

Helen Ward (HW)

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

John Walsh (JW)

Sponsor:

Lucy Parker

Research Governance Manager

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Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

Aim

To explore missed opportunities for HIV testing and factors contributing to late presentation of HIV in patients newly diagnosed with HIV in North West London.

Objectives

New HIV diagnosis

1. To explore missed opportunities for earlier HIV testing in those diagnosed with HIV through investigator-administered structured questionnaires.
2. To understand factors that contribute to the late detection of HIV using information gathered from in-depth interviews with patients relating to their attitudes and ideas around HIV testing.

Health Provider

1. To explore missed opportunities for earlier HIV testing by those able to offer HIV testing to patients through the use of self-administered questionnaires.
2. To understand health provider factors that contribute to the late detection of HIV using information gathered from focus-group interviews with health providers relating to their attitudes and ideas around HIV testing.

Methods

Study Design

This study is in two parts. The **New HIV diagnosis** aspect of the study is a cross-sectional survey of new HIV diagnosis patients made at Imperial College Healthcare NHS Trust (ICHT) from 16th July 2012 to

15th July 2013. The **Health Provider** aspect of the study will include a cross-sectional survey of staff within ICHT able to offer HIV testing.

New HIV diagnosis

a. Descriptive analysis of data collected from investigator-administered New HIV diagnosis questionnaires including information relating to previous ill health, prior contact with healthcare services and testing history to assess and compare the characteristics of late, very late and early presenters within the trust.
b. In-depth interview with 15-30 patients newly diagnosed with HIV; including late, very late are early presenters. Topics covered will include attitudes to HIV and AIDS, HIV testing and experiences with healthcare services and health providers.

Health Provider

a. Descriptive analysis of data collected from self-administered Health Provider questionnaire on knowledge of testing guidelines and prior HIV testing experience to asses testing practices amongst health providers.
b. 2-5 focus-group interviews with health providers able to offer HIV tests; including primary care practitioners, general medicine physicians and nurses. Topics covered will include attitudes to HIV/AIDS, HIV testing and prior experiences with patients testing for HIV.

Setting and recruitment

New HIV Diagnosis

Those newly diagnosed with HIV will be recruited from within ICHT. All patients newly diagnosed with HIV within the trust are referred to St Mary's Hospital via the CNS and these will also be asked to participate in our study at their local site (Hammersmith, Charing Cross or Queen Charlotte's and Chelsea). Recruitment will take place in the period from 16th July 2012 to 15th July 2013.

Participant information sheets will be offered to patients after diagnosis and at least two further clinic attendances. Patients will be asked to read the participant information sheet outlining the study and what they will be asked to do. The participant information sheet will explain that all information given in the questionnaire is completely confidential, that patient participation is non-compulsory and that patient care will not be impacted upon in anyway by their decision to participate in the study or otherwise. Those agreeing to take part in the study will sign a consent form and will then be asked to complete the New HIV diagnosis questionnaire in the department or clinic they are in along with the investigator.

In-depth interviews with 15-30 of the newly HIV diagnosed patients will take place after they are identified and appropriately referred into care. They will take place either on the hospital ward where they are admitted or in the HIV clinic when they attend their appointments within three months of diagnosis. Those agreeing to take part in the interview will have their interview in a private room with only the investigator and patient present. Interviews will be audio-taped for later transcription and analysis.

Health Provider

Health providers will be recruited from hospitals, general practices and clinics within the Imperial College Trust. They will be approached to participate by email in the period from July to August 2012 and will be sent the questionnaire directly to complete and return electronically to the research team.

2-5 focus-group discussions (involving 7-40 health providers) will take place in the hospital ward, clinic or surgery where they work. Staff will be asked to read a participant information sheet outlining the study and what the focus group session will entail. The sheet will explain that all matters discussed within in the focus group will be completely confidential and that it is important that the confidentiality of others is respected by all participants, that staff participation is non-compulsory and that they will not be impacted upon in other anyway by their participation in the study. Staff will then be asked for their consent to participate in the focus group by the investigator and if they agree the session will take place in a private room. The session will be audio-taped for later transcription and analysis.

Subjects

Subjects recruited will be New HIV diagnosis patients, Late presentation patients and Very late presentation patients and Health Provider. Defined as follows:

New HIV diagnosis - Any patient >15 years old, within the Imperial College Trust, who tests positive for HIV and who was not previously known to be HIV positive.

Late presentation patients - A new HIV diagnosis with a $CD4^+$ cell count of <350 cells/mm^3, or a new HIV diagnosis with an HIV related disease (table1.) or a new HIV diagnosis who commences antiretroviral therapy within 3 months of diagnosis.

Very late presentation patients – A late presentation with a $CD4^+$ cell count of <200 cells/mm^3.

Health Provider - A health provider working in an Imperial College Healthcare NHS Trust clinic, hospital or surgery able offer and HIV test and registered on the central trust database of employees.

Recruitment

New HIV diagnosis

All patients newly diagnosed with HIV are referred through the sexual health in practice (SHIP) teams or the Clinical nursing specialists (CNS) for a follow up appointment at St Mary's hospital. These teams will approach patients eligible for participation and offer them a participant information sheet and consent form to take away and read within the first two to three months after diagnosis. In-patients will be approached by the medical team in whose care they are in. 15 year olds deemed competent by their doctor will be consented independently and parental consent will be obtained from those who are not.

Health Provider

Using a centralised Imperial College Trust database of all staff working within the trust a selection of health providers will be randomly identified for participation. Health providers identified as able to offer HIV testing by their job title and description will be contacted regarding participation. 500 health providers will be contacted, anticipating a minimum response rate of 20%. The 'Health Provider Questionnaire' will be sent to these individuals directly via email.

Instruments

1. Study participant information sheet and consent form – Patient
2. Study participant information sheet and consent form - Provider
3. New HIV Diagnosis Questionnaire
4. Topic guide for in-depth interview with New HIV diagnosis
5. Health Provider Questionnaire
6. Topic guide for focus-group sessions with health providers

Data handling

Information collected from the investigator-administered patient questionnaire and the investigator led in-depth patient interview will be anonymised i.e. no unique information such as name, address or date of birth will be recorded for use outside of trust premises. Past patient medical records of all New HIV diagnosis patients will be reviewed to corroborate information provided by the patient and for completeness of information.

All patients testing positive for HIV will already have a unique patient number assigned to them. The patient numbers will be used solely to follow up the patient in order to:

a. To assess their $CD4^+$ cell count at time of diagnosis;

b. Identify that they have tested HIV positive and therefore administer the otherwise anonymous questionnaire;

c. Identify those that have tested HIV positive and presented late or very late in order to complete the otherwise anonymous in-depth interview;

d. Identify past medical records to corroborate information collected from self-administered questionnaires.

Following collection of these data, patient numbers will be replaced with a new study code, unlinked to the patient number. Patient numbers will be discarded from any information collected following recoding of data.

Up until the point that the data is recoded it will be kept in original NHS, protected databases on trust premises. After recoding it will be moved onto secure, password protected documents in the possession of investigator RE, for analysis. Investigators GC, HW and JW will also have access to the password protected documents.

Data analysis

Three quantitative and one qualitative method of analyses will be conducted for New HIV diagnosis patients and Health Providers.

New HIV diagnosis

Quantitative analysis of questionnaire results:

a. Descriptive statistics will be used to compare the questionnaire response between HIV groups. Differences in demographics, risk profile and healthcare contact between early, late and very late presenters will be assessed to identify patterns of healthcare contact.

b. Comparisons of the questionnaire response between the HIV groups will be made using chi-square tests (for categorical variables) and ANOVA or nonparametric Kruskal Wallis rank tests (for continuous variables).

c. Multiple multinomial logistic regression will be used to adjust the model for the most important factors where the reference category will be earlier HIV diagnosis.

Qualitative analysis of interview results:

d. A constant comparative analysis technique using a thematic approach will be used to analyse the results of interviews. This will explore attitudes to HIV/AIDS and prior experiences with health services and health providers and attempt to identify common themes in factors contributing to late diagnosis compared to earlier diagnosis in new HIV diagnosis patients. The process will be iterative

with data analysis continuing alongside data collection and data collection will be discontinued once analysis shows that thematic saturation has been reached.

Health Provider

Quantitative analysis of questionnaire results:

a. Descriptive statistics will be used to compare the questionnaire response between rates for testing. Differences in speciality, occupation and other variables in higher rates of testing compared to lower rates of testing will be assessed to identify testing patterns in health providers.

b. Comparisons of the questionnaire response between health providers offering different rates of testing will be made using chi-square testis (for categorical variables) and ANOVA or nonparametric Kruskal Wallis rank test (for continuous variables).

c. Multiple multinomial logistic regression will be used to adjust the model for the most important factors where the reference category will be a higher rate of testing.

Qualitative analysis of interview results:

A constant comparative analysis technique using a thematic approach will be used to analyse the results of focus-group interviews. This will explore attitudes to HIV/AIDS and prior testing experiences and attempt to identify common themes in factors contributing to higher compared to lower rates of testing. . The process will be iterative with data analysis continuing alongside data collection and data collection will be discontinued once analysis shows that thematic saturation has been reached.

Consent

Consent to enter the study will be sought from each participant after a full explanation has been given. Signed participant consent will be obtained. The right of the participant to refuse to participate without giving reasons will be respected. All participants are free to withdraw at any time from the study without giving reasons and without prejudicing further treatment.

Indemnity

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

Audits

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

Study Management

The day-to-day management of the study will be co-ordinated through Rahma Elmahdi (rahma.elmahdi07@imperial.ac.uk).

Ethical approval

Ethical approval will be required for all aspects of this study and will be made to NHS REC, R&D for review and an application will be made to NIHR Clinical Research Network for support.

Appendix K: Female and Male Questionnaire Template

Female Questionnaire

Study Title: Missed HIV Study: Missed Testing for HIV

Missed opportunities for testing and factors contributing to late presentation of HIV in North West London

Chief Investigators:

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Sponsor:

Lucy Parker

Research Governance Manager

510A, 5th Floor, Lab Block

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Fulham Palace Road

W6 8R

Ethics Ref: 12/LO/0779

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

We are conducting a study on missed opportunities for testing and late HIV diagnosis in North West London. We are doing this in the hope of identifying areas where HIV testing was missed and understanding how this can be reduced to improve early diagnosis of HIV infection in patients.

This questionnaire will ask you a number of questions about your contact with healthcare services, previous HIV testing and your general health. The questionnaire will also ask you questions regarding where you may have been at risk of HIV exposure in the past, including questions about your sexual behaviour, with a particular focus on the last 6 months.

Please do not be offended if some of the questions seem strange or inappropriate to you. They are important for our study and for this reason the more questions you answer the more valuable the information you provide is for our analysis. If however you do not wish to answer specific questions, please leave them blank.

All information collected from this questionnaire is strictly confidential, will not be traced back to you and will be kept separately from your medical records.

Section A: About You

1. How old are you?

   _____

2. Which country were you born in?

   _____

3. If you were not born in the UK, how long have you lived in the UK?

_____ / _____ (month/year)

4. How would you describe your sexuality?

- ☐ Homosexual
- ☐ Heterosexual
- ☐ Bisexual

5. What is your current marital status?

- ☐ Single
- ☐ Married
- ☐ Divorced/Widowed
- ☐ Long-term relationship

6. How many children do you have?

_____

Section B: About your contact with healthcare services

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

1. Are you registered with a GP?

☐ Yes

☐ No

If yes, How long have you been registered with your current GP?

_____ / _____ (month/year)

2. Have you visited your GP in the last year?

☐ Yes

☐ No

3. Have you visited a specialist in the hospital in the last year?

☐ Yes

☐ No

If yes, which department or which type of specialist did you visit?

_____

4. Have you been admitted to hospital in the last year?

- ☐ Yes
- ☐ No

If yes, which department were you admitted to?

_____

5. When was the last time you had an HIV test before testing positive for HIV?

_____

6. If you have ever been offered an HIV test before testing positive for HIV, where was this test offered?

- ☐ GP
- ☐ Sexual health clinic
- ☐ Antenatal care services
- ☐ Medical admissions in the hospital
- ☐ Other, Please specify _____

If so, who requested the HIV test?

- ☐ Yourself

- ☐ Doctor
- ☐ Nurse
- ☐ Midwife

7. What was the name of the hospital or clinic where this test was carried out?

_____

8. Have you ever refused an HIV test in the past?

- ☐ Yes
- ☐ No

If yes, please state your reasons for refusing the offer of a test?

_____

_____

Section C: About your general health

1. Have you felt unwell in the last year?

- ☐ Yes
- ☐ No

If yes, did you seek advice, treatment or medical care for this?

- ☐ Yes
- ☐ No

If yes, where did you go to get this?

- ☐ Pharmacy
- ☐ GP
- ☐ Hospital
- ☐ Sexual health clinic
- ☐ Other, if so, please specify _____

For every time you have felt unwell and had contact with health services in the last year, please give the following details:

Symptoms	Type of health service you had contact with	Tests/ interventions you underwent	
	Diagnosis	Treatment offered	HIV test offered

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Section D. About your risk of exposure to HIV

1. Have you ever been diagnosed with a sexually transmitted infection?

☐ Yes

☐ No

If yes, please mark yes or no for the following and write an approximate date (to the nearest month and year)

a. Chlamydia Yes/No

_____ /_____ (month/year)

b. Gonorrhoea Yes/No

_____ /_____ (month/year)

c. Herpes Yes/No

_____ /_____ (month/year)

d. Syphilis Yes/No

_____ /_____ (month/year)

e. Warts Yes/No

_____ /_____ (month/year)

2. Have you ever been given post-exposure prophylaxis (PEP) by a doctor because you may have been exposed to HIV?

□ Yes

□ No

3. Have you ever received a blood transfusion?

□ Yes

□ No

If yes, please state the date on which you received your first blood transfusion.

_____ / _____ (month/year)

4. Have you ever injected drugs?

☐ Yes

☐ No

If yes, when was the last time you injected drugs?

_____ / _____ (month/year)

Have you ever shared needles?

☐ Yes

☐ No

Section E: About your recent sexual history

1. In the last 6 months have you had a casual male sexual partner (a casual partner is someone that you have had sex with on only one occasion.)

☐ Yes

☐ No

If yes, how many casual male sexual partners have you had in the last 6 months?

_____ (number)

How many casual male partners have you had unprotected vaginal or anal sex with in the last 6 months? (Unprotected sex is when a condom is not being used during intercourse.)

_____ (number)

Is male partner that you have had sex with in the last 6 months (casual or otherwise) known to be HIV positive?

☐ Yes

☐ No

2. Please state the county of origin of any male sexual partner (both casual and regular) that you have had unprotected sex with in the last 6 months.

_____

Section F: Further participation

Would you be willing to help us further with our research and allow us to contact you regarding participation in a confidential interview about your experience with testing for HIV at a time convenient to you? If so, please provide a means of contacting you regarding this.

_____

You have now finished!

Thank you for taking the time to complete this questionnaire.

Male Questionnaire

Study Title: Missed HIV Study: Missed Testing for HIV

Missed opportunities for testing and factors contributing to late presentation of HIV in North West London

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Collaborators:

Helen Ward (HW)

John Walsh (JW)

Sponsor:

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510A, 5th Floor, Lab Block

Charing Cross Hospital

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

Fulham Palace Road W6 8RF

Ethics Ref: 12/LO/0779

We are conducting a study on missed opportunities for testing and late HIV diagnosis in North West London. We are doing this in the hope of identifying areas where HIV testing was missed and understanding how this can reduced to improve early diagnosis of HIV infection in patients.

This questionnaire will ask you a number of questions about your contact with healthcare services, previous HIV testing and your general health. The questionnaire will also ask you questions regarding where you may have been at risk of HIV exposure in the past, including questions about your sexual behaviour, with a particular focus on the last 6 months.

Please do not be offended if some of the questions seem strange or inappropriate to you. They are important for our study and for this reason the more questions you answer the more valuable the information you provide is for our analysis. If however you do not wish to answer specific questions, please leave them blank.

All information collected from this questionnaire is strictly confidential, will not be traced back to you and will be kept separately from your medical records.

Section A: About You

1. **How old are you?**

   _____

2. **Which country were you born in?**

   _____

3. **If you were not born in the UK, how long have you lived in the UK?**

   _____ / _____ *(month/year)*

4. **How would you describe your sexuality?**

   Homosexual

   Heterosexual

   Bisexual

5. **What is your current marital status?**

   Single

   Married

   Divorced/Widowed

   Long-term relationship

6. **How many children do you have?**

   _____

Section B: About your contact with healthcare services

1. **Are you registered with a GP?**

   Yes

   No

   If yes, how long have you been registered with you**r current** GP?

   _____ / _____ *(month/year)*

2. **Have you visited your GP in the last year?**

   Yes

   No

3. **Have you visited a specialist in the hospital in the last year?**

   Yes

   No

   If yes, which department or which type of specialist did you visit?

   _____

4. **Have you been admitted to hospital in the last year?**

   Yes

No

If yes, which department were you admitted to?

_____

5. **When was the last time you had an HIV test before testing positive for HIV?**

In the last 6 months

In the last year

In the last 5 years

Never

If you have ever been offered an HIV test before testing positive for HIV, where was this test offered?

GP

Sexual health clinic

Antenatal care services

Medical admissions in the hospital

Other, Please specify _____

Who requested the HIV test?

Yourself

Doctor

Nurse

Midwife

What was the name of the hospital or clinic where this test was carried out?

6. **Have you ever refused an HIV test in the past?**

Yes

No

If yes, please state your reasons for refusing the offer of a test?

_____

_____

_____

<u>Section C: About your general health</u>

1. **Have you felt unwell in the last year?**

Yes

No

If yes, did you seek advice, treatment or medical care for this?

Yes

No

If yes, where did you go to get this?

Pharmacy

GP

Hospital

Sexual health clinic

Other, if so, please specify _____

For every time you have felt unwell and had contact with health services in the last year, please give the following details:

Symptoms	**Type of health service you had contact with**	**Tests/ interventions you underwent**	**Diagnosis**	**Treatment offered**	**HIV test offered**

<u>Section D. About your risk of exposure to HIV</u>

1. **Have you ever been diagnosed with a sexually transmitted infection?**

Yes

No

If yes, please mark yes or no for the following and write an approximate date *(to the nearest month and year)*

a. Chlamydia	Yes/No	_____ /_____ *(month/year)*
b. Gonorrhoea	Yes/No	_____ /_____ *(month/year)*
c. Herpes	Yes/No	_____ /_____ *(month/year)*
d. Syphilis	Yes/No	_____ /_____ *(month/year)*
e. Warts	Yes/No	_____ /_____ *(month/year)*

2. **Have you ever been given post-exposure prophylaxis (PEP) by a doctor because you may have been exposed to HIV?**

   Yes

   No

3. **Have you ever received a blood transfusion?**

   Yes

   No

   If yes, please state the date on which you received your first blood transfusion.

   _____ / _____ *(month/year)*

4. **Have you ever injected drugs?**

Yes

No

If yes, when was the last time you injected drugs?

_____ / _____ *(month/year)*

Have you ever shared needles?

Yes

No

<u>Section E: About your recent sexual history</u>

1. **Do you have sex with women?**

Yes

No

If no, please move on to question 4.

2. **In the last 6 months have you had a casual female sexual partner** (a casual sexual partner is someone that you have had sex with on only one occasion.)

Yes

No

If yes, how many casual female sexual partners have you had in the last 6 months?

_____ *(number)*

How many casual female partners have you had unprotected vaginal or anal sex with in the last 6 months? (Unprotected sex is when a condom is not being used during intercourse.)

_____ *(number)*

If you have had unprotected sex with a casual female partner, were any of the casual female partners you have had unprotected sex with known to be HIV positive?

Yes

No

3. **Please state the county of origin of any female sexual partner (both casual and regular) that you have had <u>unprotected</u> sex with in the last 6 months.**

_____

4. **Have you ever had sex with a man?**

Yes

No

If no, please move on to Section F.

In the last 6 months have you had a casual male sexual partner (a casual partner is someone that you have had sex with on only one occasion.)

Yes

No

If yes, how many casual male sexual partners have you had in the last 6 months?

_____ *(number)*

How many casual male partners have you had unprotected anal sex with in the last 6 months? (Unprotected sex is when a condom is not being used during intercourse.)

_____ *(number)*

If you have had unprotected sex with a casual male partner, were any of the casual male partners you have had unprotected sex with known to be HIV positive?

Yes

No

5. **Please state the county of origin of any male sexual partner (both casual and regular) that you have had <u>unprotected</u> sex with in the last 6 months.**

   _____

<u>Section F: Further participation</u>

Would you be willing to help us further with our research and allow us to contact you regarding participation in a confidential interview about your experience with testing for HIV at a time convenient to you? If so, please provide a means of contacting you regarding this.

_____

You have now finished!

Thank you for taking the time to complete this questionnaire.

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

Appendix L: Participant Information Sheet and Consent form

Missed HIV Study: Missed Testing for HIV

Missed opportunities for testing and factors contributing to late presentation of HIV in North WestLondon

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Rahma Elmahdi

Infectious Disease Epidemiology

Praed Street

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W2 1NY

Sponsor:

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

Ethics Ref: 12/LO/0779

You are being invited to take part in a research study on late presentation and missed opportunities for testing in HIV in North West London. Before deciding to take part you need to understand why we want you to participate and what it will involve. Please take the time to read the information provided carefully.

PURPOSE OF THE STUDY

- We know that up to 30% of people living with HIV in the UK are not aware they are infected.
- We also know that half of all new HIV diagnoses every year are in people at a late stage of infection.
- This study aims to investigate why people do not receive an HIV test earlier and are consequently diagnosed at a later stage of infection.
- We are collecting this information in the hope of improving testing practices for HIV in the future.
- The findings from this study will also be going towards an educational qualification.

WHY YOU HAVE BEEN INVITED TO PARTICIPATE

- You have been invited to participate in the study because you are a patient in our area who has recently been diagnosed with HIV.
- For this reason we would like to invite you to complete a questionnaire with a researcher and possibly also have an interview with a researcher.
- Taking part in the study is voluntary. If you agree to participate you will be asked to sign a consent form indicating that you wish to do so.
- You are free to withdraw from the study at any point.
- If you chose not to take part in the study we would be grateful if you could tell us your reasons for refusing to do so however, this is also optional.

WHAT YOU WILL BE ASKED TO DO

- You will be asked to complete a 'New HIV Diagnosis Questionnaire'. The questionnaire will ask you a number of questions about your contact with healthcare services, previous HIV testing and your general health.
- This will take no more than half an hour and will be completed with a researcher.
- In addition to this, if you indicate your interest in further participation in the study, we may ask you to take part in an interview with a researcher. The interview will be on some of the topics covered in the questionnaire but will allow you to provide more detailed information on your personal experiences.
- This will take no longer than 2 hours and will be carried out by the study investigator.
- Any travel expenses incurred in order to participate in the study will be reimbursed to you. Please retain receipts of travel purchase in order to reclaim the cost.
- If you decide to participate and complete the questionnaire we would like to offer you a £10 voucher and if you would further like to participate and complete the interview another £10 voucher would be offered to you as a thank you for giving up your time to take part.

WHICH TOPICS WILL BE COVERED

The questionnaire will be comprised of some questions regarding the following:

- Contact with healthcare services
- Your general health
- Your risk of HIV exposure
- Your recent sexual history

The questionnaire will be given to you at your next attendance to the clinic or after you are admitted to the ward where a researcher will help you complete it.

The interview will allow you to provide an in-depth response to the following:

- Your health
- Your previous experience and ideas around HIV testing and healthcare services
- Your previous experiences and ideas around HIV testing and health professionals

The interview will be informal with very few questions but will provide you with the opportunity to give detailed responses. The interview will be recorded. The researcher will not be taking written notes but will be making a written copy of the recording (transcription) for later analysis. This copy will be anonymised with only a study number and none of your personal details retained. After this process the recording will be destroyed. If there is any subject you are uncomfortable talking about then you should not feel obliged to do so and you can stop at any point.

YOUR RESPONSIBILITIES

You will have a copy of this information sheet and the consent form. If you agree to participate then you sign the consent form and return it on your next visit where you will be given the questionnaire and may be invited to take part in the interview.

BENEFITS AND RISKS OF PARTICIPATION

- You may find it helpful to have a chance to talk about your experiences.
- However, it is important to understand that the aim of the questionnaires and interviews is to collect information for the study in the hope of improving testing practices for HIV in the future with guidance from real life experiences from patients.
- They have not been designed to provide psychological support. If you have any concerns regarding your physical or mental health you should contact your Clinical Nurse Specialist or Doctor for advice or help.

CONFIDENTIALITY

- All information given in the study is completely confidential and will be anonymised i.e. no unique information such as full name, address or date of birth will be requested or recorded.

- Only the researchers and representatives of regulatory authorities and ethics committees may have direct access to this data.
- Any information transferred electronically (e.g. by e-mail) will be coded to protect your identity. All computer records will be password protected.
- Audio-recordings will be destroyed after transcription.
- Unidentifiable study documentation may be securely stored for up to 10 years by Imperial College London.

RESULTS OF THE STUDY

- The results of the study will not be known until several months after collection of all information.
- The results may be presented at medical conferences and published in scientific journals.
- No material which could identify you will be used in any reports.

IF SOMETHING GOES WRONG

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Dr Graham Cooke, graham.cooke@imperial.ac.uk). The normal National Health Service complaint complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Compliance Office.

STUDY REVIEW

This study has received ethical approval from NHS research and development and Research Ethics Committee.

CONTACT DETAILS

If you need any further information or have any questions or concerns about any aspect of the study please contact Rahma Elmahdi by phone on 020 7594 3218 or email at rahma.elmahdi07@imperial.ac.uk

Thank you for taking the time to read this sheet

Do you wish to participate in the study?

If no, can you please use the space below to specify why (this is optional)

If Yes, Please read and sign the attached Consent Form

Missed HIV Study: Missed Testing for HIV

Missed opportunities for testing and factors contributing to late presentation of HIV in North West London

CONSENT FORM

Chief investigators: Dr Graham Cooke

Please initial box

I confirm that I have read and understand the participant information sheet dated 25/06/2012 (Version 3.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
I agree to take part in the above study.	
I understand that sections of any of my medical notes may be looked at by responsible individuals from Imperial College London, Imperial College NHS Trust or from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to access my records that are relevant to this research.	

Should I additionally be asked to participate and agree to take part in the in-depth interview, I consent to being recorded for the purposes of transcription and understand that following anonymised transcription, the recording will be destroyed.

.

_____	_____	_____
Name of Patient	Date	Signature

_____	_____	_____
Name of person taking consent	Date	Signature

A copy of the signed Consent form will be given to the Participant, the Investigator and a copy will be filed in the Participant's medical notes.

Appendix M: Complete STATA code for analysis of Missed HIV study data

```
import excel "C:\Users\Rahma Elmahdi\Desktop\missedhivSTATA.xlsx", sheet("Sheet1") firstrow

d

lab define chlam 0"No" 1"Yes"

lab values chlam chlam

tab chlam

lab define countryorigin 0"UK" 1"Europe"  2"Abroad"

lab values countryorigin countryorigin

tab countryorigin

lab define ethnic 0"White British" 1"White Other" 2"Mixed" 3"Asian" 4"Black African" 5"Black Caribbean"
6"Other/Unknown"

lab values ethnic ethnic

tab ethnic

lab define gono 0"No" 1"Yes"

lab values gono gono

tab gono

lab define herp 0"No" 1"Yes"lab values herp herp

tab herp

lab define hospitalspeciality 0"GUM/SH" 1"Cardiology" 2"Gastroenterology" 3"A&E"
4"Urology"5"Respiratory" 6"Psychiatry" 7"Stroke" 8"Renal" 9"Oncology" 10"Hepatology" 11"AMU"
12"Surgery" 13"ENT" 14"Orthopaedics"
```

lab values hospitalspeciality hospitalspeciality

tab hospitalspeciality

lab define hospitalvisitspeciality 0"GUM/SH" 1"Cardiology" 2"Gastroenterology" 3"A&E" 4"Urology" 5"Respiratory" 6"Psychiatry" 7"Stroke" 8"Renal" 9"Oncology" 10"Hepatology" 11"AMU"

lab values hospitalvisitspeciality hospitalvisitspeciality

tab hospitalvisitspeciality

lab define idu 0"No" 1"Yes"

lab values idu idu

tab idu

lab define iduneedleshare 0"No" 1"Yes"

lab values iduneedleshare iduneedleshare

tab iduneedleshare

lab define locationdx 0"GUM/HIV" 1"ANC" 2"In-patient/OPD" 3"A&E" 4"GP" 5"Other"

lab values locationdx locationdx

tab locationdx

lab define marital 0"Single" 1"Married" 2"Divorced/Separated/Widowded" 3"Long-term Relationship" 4"Long-term Relationship"

lab values marital marital

tab marital

lab define nation 0"UK" 1"Europe" 2"Abroad"

lab values nation nation

tab nation

```
lab define othersti 0"No" 1"Yes"

lab values othersti othersti

tab othersti

lab define sex 0"Female" 1"Male"

lab values sex sex

tab sex

lab define sexmen 0"No" 1"Yes"

lab values sexmen sexmen

tab sexmen

lab define sexmenbirth 0"UK" 1"Europe" 2"Abroad" 3"Unknown"

lab values sexmenbirth sexmenbirth

tab sexmenbirth

lab define sexmencasual 0"No" 1"Yes"

lab values sexmencasual sexmencasual

tab sexmencasual

lab define sexmenhiv 0"No" 1"Yes" 2"Don't Know"

lab values sexmenhiv sexmenhiv

tab sexmenhiv

lab define sexual 0"MSM" 1"Heterosexual"

lab values sexual sexual

tab sexual
```

```
lab define sexuality 0"MSM" 1"Bisexual" 2"Heterosexual"

lab values sexuality sexuality

tab sexuality

lab define sexwomen 0"No" 1"Yes"

lab values sexwomen sexwomen

tab sexwomen

lab define sexwomenbirth 0"UK" 1"Europe" 2"Abroad"

lab values sexwomenbirth sexwomenbirth

tab sexwomenbirth

lab define sexwomencasual 0"No" 1"Yes"

lab values sexwomencasual sexwomencasual

tab sexwomencasual

lab define sexwomenhiv 0"No" 1"Yes" 2"Don't Know"

lab values sexwomenhiv sexwomenhiv

tab sexwomenhiv

lab define sti 0"No" 1"Yes"

lab values sti sti

tab sti

lab define syph 0"No" 1"Yes"

lab values syph syph

tab syph
```

lab define testrefusal 0"No" 1"Yes"

lab values testrefusal testrefusal

tab testrefusal

lab define testwhere 1"GP" 2"GUM/SH" 3"AMU" 4"ANC" 5"Other" 6"A&E"

lab values testwhere testwhere

tab testwhere

lab define testwho 0"Yourself" 1"Doctor or Nurse" 2"Doctor or Nurse"

lab values testwho testwho

tab testwho

lab define transfusion 0"No" 1"Yes"lab values transfusion transfusion

tab transfusion

lab define warts 0"No" 1"Yes"

lab values warts warts

tab warts

lab define pep 0"No" 1"Yes"

lab values pep pep

tab pep

lab define carewhere 0"Pharmacy" 1"GP" 2"GUM/SH" 3"AMU" 4"ANC" 5"Other" 6"A&E" 7"None"

lab values carewhere carewhere

tab carewhere

lab define illwhere 0"Pharmacy" 1"GP" 2"GUM/SH" 3"AMU" 4"ANC" 5"Other" 6"A&E" 7"None"

```
lab values illwhere illwhere

tab illwhere

lab define illwhere2 0"Pharmacy" 1"GP" 2"GUM/SH" 3"AMU" 4"ANC" 5"Other" 6"A&E" 7"None"

lab values illwhere2 illwhere2

tab illwhere2

lab define illwhere3 0"Pharmacy" 1"GP" 2"GUM/SH" 3"AMU" 4"ANC" 5"Other" 6"A&E" 7"None"

lab values illwhere3 illwhere3

tab illwhere3

gen agedays = datedx-dob

gen age = agedays/365.2

gen logviral = log(viralcopies)

gen agecat = age

replace agecat =0 if age>=50

replace agecat =1 if age <50

replace agecat=2 if age<40

replace agecat =3 if age<25

lab define agecat 0">=50" 1"40-49" 2"25-39" 3"18-24"

labe values agecat agecat

tab agecat

gen earlylate =1 if cd4 <2000

replace earlylate = 0 if cd4<350
```

```
replace earlylate = 1 if cd4 >=350

tab earlylate

lab define earlylate 0"late(cd4<350cells/mm3)" 1"early(cd4>=350/mm3"

lab values earlylate earlylate

tab earlylate

sum cd4 if earlylate==0,d

sum cd4 if earlylate == 1, d

sum cd4, d

tab sex

tab sex if earlylate ==0

tab sex if earlylate == 1

gen ethcat = .

replace ethcat = 0 if ethnic == 0

replace ethcat = 0 if ethnic == 1

replace ethcat = 1 if ethnic ==3

replace ethcat = 2 if ethnic == 4

replace ethcat = 2 if ethnic == 5

replace ethcat = 3 if ethnic == 6

replace ethcat = 3 if ethnic == 2

lab define ethcat 0"White" 1"Asian" 2"Black" 3"Other/Unknown"

lab values ethcat ethcat
```

```
replace ethcat = 3 if ethnic == .

tab ethcat

tab ethcat if earlylate == 0

tab ethcat if earlylate == 1

tab sexual

tab sexual if earlylate == 0

tab sexual if earlylate == 1

tab agecat

tab agecat if earlylate == 0

tab agecat if earlylate == 1

sum age, d

sum age if earlylate == 0, d

sum age if earlylate == 1, d

twoway scatter logviral age if sexual == 0

sum logviral, d

sum logviral if earlylate ==0, d

sum logviral if earlylate ==1, d

graph box logviral, over(earlylate)

tab countryorigin

sum lasttestneg

sum lasttestneg, d
```

```
tab locationdx

gen testneg = .

replace testneg = lasttestneg-datedx

replace testneg = datedx-lasttestneg

gen testnegdays = testneg/365.2

gen testnegmonth =testnegdays*12

sum testnegmonth, d

di 20/87

tab ethnic if testnegmonth == 0

tab sexuality if testnegmonth==0

tab sex if testnegmonth ==0

tab agecat if testnegmont==0

gen testnever=.

replace testnever = 0 if testnegmonth==0

replace testnever = 1 if testnegmonth >0

drop testnever

gen testnever = .

sum testnegmonth,

replace testnever = 0 if testnegmonth <293.5

replace testnever = 1 if testnegmonth == 0

tab testnever
```

```
lab define testnever 0"tested" 1"nevertested"

lab values testnever testnever

tab testnever

tab testnever sex, chi2

tab testnever ethnic, exact

tab testnever sex, exact

tab testnever sexuality, exact

tab testnever sexual, exact

tab testnever sexual, chi2

tab testnever sex, chi2

tab testnever ethcat, chi2

xi: logistic testnever i.sex i.sexual i.ethcat, or

xi: logistic testnever i.ethcat, or

xi: logistic testnever i.sexual, or

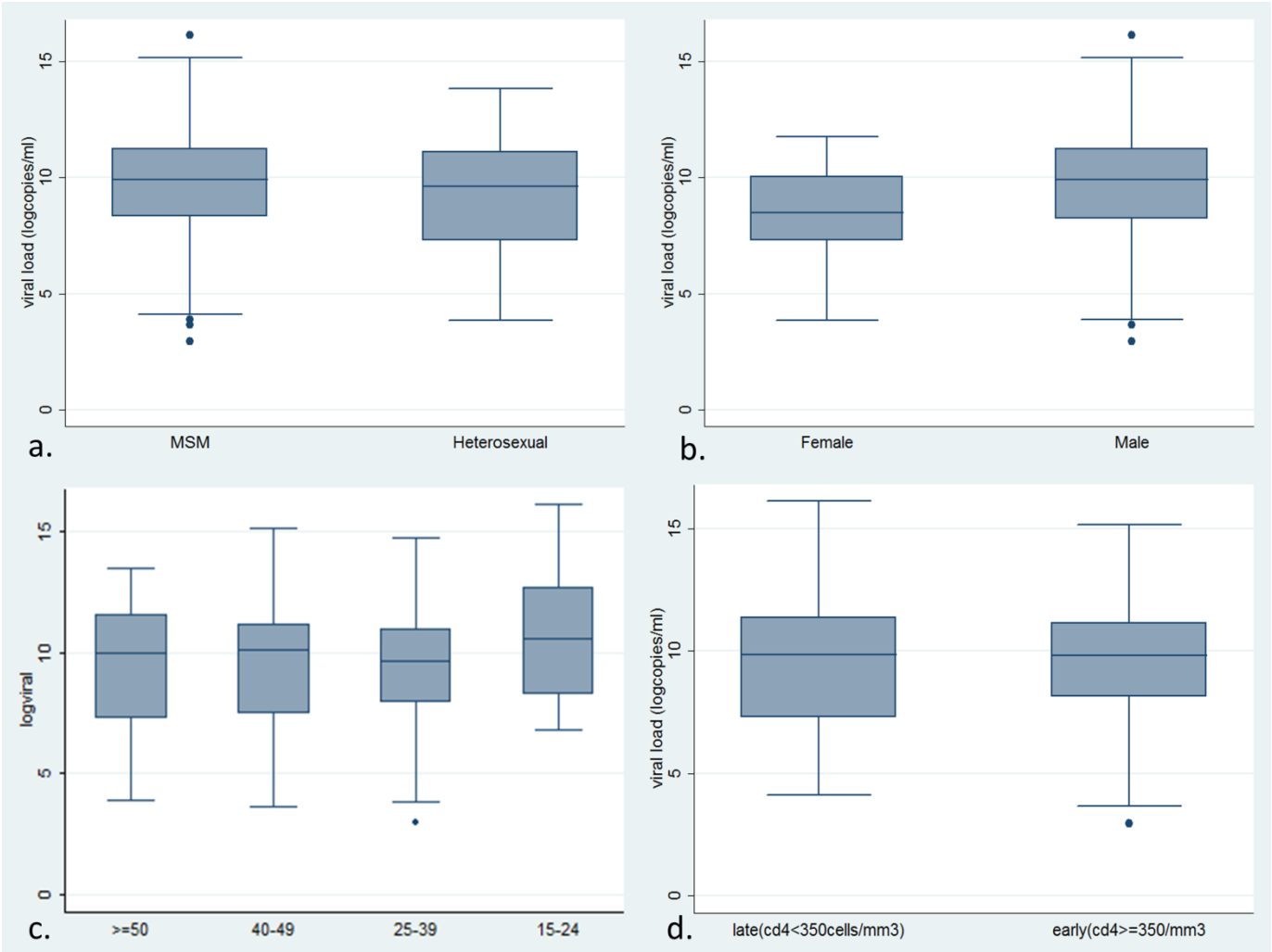
xi: logistic testnever i.sex, or

gen sexrisk = .

replace sexrisk = 0 if sex == 1

log close
```

Appendix N: Viral load (logcopies/ml) of patients newly diagnosed with HIV by a) sexual risk, b) sex, c) age group and d) early/late diagnosis



Appendix O: Topic guide for semi-structured interview with New HIV diagnosis patient

Aim: To understand why some people present later in HIV infection than others by identifying factors which impact on HIV testing.

You will gather responses in-line with the questionnaire from all new HIV diagnosis patients. The topic guide is based on some of the questions in the questionnaire although there is scope to gather more detailed and specific responses around issues that are more pertinent to patients' day to day lives.

Before the interview

- Request permission to record the interview and show the patient the device.
- Explain why the interview is being recorded and that the recording will not heard by anyone except the investigator.
- Reassure the patient that everything discussed will remain confidential.
- Request that the respondent is honest when answering the questions and that they attempt to answer the interview questions as fully as possible.
- Explain that the purpose of the interview is to develop an idea of why the patient has been diagnosed with HIV at the time they have and in order to do this you will be enquiring about the patient's attitude to HIV/AIDS and their ideas around health services and providers.
- Explain that you will not be taking written notes, however you will be making a written copy of the recording for later analysis. This copy will be anonymised with only a study number with no identifiable details.
- Clarify that if there is any subject the patient is uncomfortable talking about then they should not feel obliged to do so and that they can stop at any point should they wish to take a break or stop the interview.
- Check that the patient is comfortable with this and wishes to continue.
- Clearly signpost the different topic areas being covered and summarise what the patient has said periodically during the course of the interview.

Topics to cover

- Introduction
- Attitudes to HIV/AIDS
- Ideas around healthcare services
- Ideas around healthcare providers
- Summary

Introduction

Why are you here?

What's your life at home like?

What do you do?

What has your general state of health been like over the last year?

Ideas around HIV/AIDS

What were your thoughts on HIV and AIDS before being diagnosed?

What did you think the risks for acquiring HIV infection were?

Have you ever had reason to consider yourself at risk of acquiring the infection?

What did you think would be the impact of testing and being diagnosed with HIV?

Ideas around HIV testing and healthcare services

Have you been to see your doctor recently? What was the reason for this?

Tell me about any personal constraints you have felt in seeking healthcare?

How have other factors had an impact on your access to healthcare?

Ideas around HIV testing and healthcare providers

Tell me about a time when you experienced reluctance to accept an offer of an HIV test? Was this due to you feeling singled out or targeted because of your lifestyle, race or sexuality?

Tell me about a time when you wanted to request an HIV test but you felt you couldn't. Tell me about how fear of a negative reaction from your doctor or nurse may have impacted on this?

How do you think fear of lack of discretion or confidentiality on part of your doctor or nurse has impacted on your decision to test for HIV in the past?

Summary

What do you think have been the most important things that we have spoken about?

What would you like to discuss in more depth?

Do you have any questions for me?

After the interview

Thank the patient for their participation and remind them of the investigator's name and contact details, should they have any further questions or concerns and wish to contact you.

Appendix P: SPIT Patient information sheet and Consent form

Patient Information Leaflet and Eligibility criteria

Study Title: SPIT Study: Saliva patient initiated testing for HIV

Feasibility and acceptability of repeat home-based HIV saliva testing using self-sampling amongst men who have sex with men

Chief Investigator Dr Sarah Fidler

Ethics Ref: 12/LO/0556

1. Invitation

You are being invited to take part in a research study which will involve looking at a different way of testing for the presence of the HIV virus. You can be taught how to take this test yourself at home. The information we obtain from this study will help us to make changes to the current way we offer repeat HIV testing. Please take time to read the following information carefully, and discuss it with others if you wish. We would like to ask you to take your own sample of saliva (from your mouth) which can be used to test for the presence of antibodies to the HIV virus. We will give you 6 test kits which you can keep at home and send in to us via the post whenever you think you would like to repeat test for HIV. This study lasts for 1 year and we would like to see you in the clinic for a final visit in a year's time.

This test measures antibodies to HIV –which means it may miss very early stages of HIV infection. This means there is a small chance that you may test 'negative' for HIV using the oral swab test but in fact have very early infection which does not show up yet using this test kit. If you have had a very recent sexual exposure that you are concerned about, or you are feeling unwell with symptoms that could possibly mean you have very early HIV infection we would encourage you to attend the clinic for assessment.

This test uses a sample of saliva to measure a protein in the saliva (antibody) that is only present in people who carry the HIV virus infection. It does not mean that there is virus in the saliva and it is highly unlikely that HIV can be passed from one person to another through saliva alone, or through kissing or mouth to mouth contact.

If you chose to take part in the study and take home these test kits it is important that you understand that these test kits are for your personal use only.

2. What is the purpose of this study?

At the moment if you wish to have a repeat HIV test it is necessary for you to attend a health care facility of some sort which is often inconvenient and time consuming. The idea of this study is to look at how easy and acceptable people find self-testing for HIV rather than having to keep coming back to a clinic.

3. Why have I been chosen?

You have been invited to take part because you have attended the GUYS @ Mary's Clinic and have had a negative test for HIV today.

4. Do I have to take part?

No. Taking part in this study is completely voluntary which means it is entirely up to you to decide whether or not to take part. Your decision will not affect your medical care or treatment in any way. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form to confirm that you understand what is involved when taking part in this study. Even if you decide to take part you are free to leave the study at any time and without giving a reason. If you withdraw, unless you object, we will still keep records relating to the treatment given to you, as this is valuable to the study. A decision to withdraw at any time, or a decision not to take part, will not affect the quality of care you receive.

5. What would happen to me if I take part?

We will ask you to have an oral swab test (a sample will be taken from inside your mouth that can be sent to the laboratory to test if you have the HIV virus) We will teach you how to take this swab yourself at home

and give you 6 sets of swabs so that over the next year you can decide when you wish to repeat test for HIV. You will be able to post the swab samples back to us in a stamped addressed envelope.

You will be asked to complete a short questionnaire at the beginning of the study and one at the end a year later.

Whenever you wish to repeat your HIV test you will take the oral swab from your mouth as you have been shown and place the swab into either the envelope provided

You will receive a text message as soon as the laboratory receive your sample to confirm to you that the sample is being tested

The results of your HIV test will be available within a maximum of 2 weeks from when you posted it and you can chose how you wish to get these results; either by a text message, phone call, email, letter or come into clinic to be told your result by a member of the research team. Test results will only be sent to you between working hours of the clinic in case you would wish to contact any of the clinical staff immediately; this means they will not be available after 7pm or at weekends.

If you run out of swabs and would like to collect more you can collect them from the clinic while the study is running, which is for one year

We will ask you to return for one final research project visit in a year's time

You are able to come along to the clinic whenever you wish in addition to taking part in this study either for Sexual health testing, HIV testing or for any other query.

6. What would happen to any samples that I give?

Blood samples that you have taken as part of your usual clinic tests will be stored in the laboratory and oral swab samples will be kept in the routine laboratory. Samples collected will be stored in the laboratory and may be used for other research studies.

Samples collected for this research would not have your name on them but would be identified by a unique number.

7. What are the possible disadvantages and risks?

The risks involved in this research are few. There is no risk of having an oral swab test and the results will be managed with very careful attention to your personal privacy, as is standard procedure. Every effort is made to keep records of personal information confidential and secure but an absolute guarantee of this can never be given. The information that you give will be stored with a code rather than your name, on a secure computer system, which will only be accessible by the few individuals that are specifically named in this study.

8. What if I want to have a sexual health check-up whilst in the study or think I may have caught a sexually transmitted infection?

You can have a sexual health check-up at any time during the study. If you think you have any symptoms it is important to have a sexual health check-up. You can telephone and book an appointment at the GUYS clinic by calling 0203 312 6790, or attend any clinic.

9. What are the possible benefits?

This research is likely to improve understanding of how best we can deliver easier access to HIV testing amongst a community of individuals who are choosing to have a test.

10. What happens when the research study stops?

The results of this research study may be presented at medical and scientific meetings or in publications. You would not be personally identified in any presentations or publications. If we find that this is a much easier way to offer repeat HIV testing we hope we request of our health authorities to continue to provide this as part of our routine HIV testing service. We will of course feedback to all our participants the main results.

11. What will happen if I don't want to carry on?

You are free to decide if you do not want to carry on with this research at any time, without giving a reason and without any effect on your future care or treatment. If you wish, all your samples and all data pertaining to you can be destroyed at any time.

12. What if something goes wrong?

Imperial College has arrangements in place to provide for harm arising from participation in the study for which Imperial College is the Research Sponsor.

13. Would my taking part in this study be kept confidential?

Confidentiality and keeping your records securely are very important parts of this research. Personal information will be kept on a computer to which access will be limited. You would also be allocated a unique number that would be used for all of the tests done on your samples and for most of the research on the information collected at the clinic. All the information necessary for the research will be used through your unique clinic number. The researchers using this information are aware of the importance of security and confidentiality even though they do not have access to personal information such as your name or address. No information will be passed to your family doctor without your consent.

14. Who is organising and funding the research?

The research is supported by the British HIV Association through funding to the Imperial College London.

15. Who has reviewed the study?

This research study has been reviewed by appropriate ethical committees in accordance with local and national regulations.

16. Complaints procedure

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the Imperial College Joint Research Compliance Office (JRCO) on 020 3311 0206 or the Patient Advice Liaison Service (PALS) on 020 3312 7777.

17. Contact for further information

If you would like more information, or if you have any problems, concerns or questions about the study, please contact the doctor looking after you or Imperial College Joint Research Compliance Office (JRCO) or Dr Alan Smith 020 3312 6853 or Dr Sarah Fidler 020 3312 6972.

Consent Form

Study Title: SPIT Study: Saliva patient initiated testing for HIV

Feasibility and acceptability of repeat home-based HIV saliva testing using self-sampling amongst men who have sex with men

Chief investigator: Dr Sarah Fidler

Please initial box

I confirm that I have read and understand the participant information sheet dated 16/4/2012 (version 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
I agree that my blood and saliva samples will be stored in the laboratory and may be used in other research studies	☐
I agree to take part in the above study.	☐

I understand that sections of any of my medical notes may be looked at by responsible individuals from Imperial College London or from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to access my records that are relevant to this research	

_____ _____ _____

Name of Patient Date Signature

_____ _____ _____

Name of person Date Signature

taking consent

A copy of the signed Consent form will be given to the Participant, the Investigator and a copy will be filed in the Participant's medical notes.

Appendix Q: Template of Baseline and End-of-study Questionnaire

Salivary Patient Initiated Testing (SPIT) study

Chief Investigator: Dr Sarah Fidler Principal Investigator: Dr Alan Smith

Chief Investigator:

Dr Sarah Fidler

Senior Lecturer/Honorary Consultant Physician

Imperial College

St Mary's Hospital

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London

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Tel: 0203 312 6972

Fax: 0203 312 6123

Email: s.fidler@imperial.ac.uk

Primary Researcher:

Ms Rahma Elmahdi

Postgraduate Research Student

Imperial College London

School of Public Health

St Mary's Hospital

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London

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Tel: 020 7594 3218

Email: rahma.elmahdi@imperial.nhs.uk

Principal Investigator:

Dr Alan Smith

Consultant Physician GUM/HIV

Imperial College NHS Trust

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London

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Tel: 0203 312 6845

Fax: 0203 312 6645

Email: alan.smith@imperial.nhs.uk

Sponsor:

Ms Lucy Parker

Research Governance Manager

Regulatory Compliance

Imperial College London and Imperial College

Healthcare NHS Trust

Room 510A

5th floor Lab Block

Charing Cross Hospital

Fulham Palace Road

W6 8RF

Tel: 0203 311 0206

Fax: 0203 311 0203

Email: lucy.parker@imperial.ac.uk

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

End of study questionnaire

We are conducting a study on the feasibility and acceptability of repeat home-based HIV saliva testing using self-sampling amongst attendees of the St Mary's gay men's sexual health (GUYS) clinic. We are doing this in the hope of identifying whether this means of testing for HIV would be of use to us in our future HIV testing practices.

This is the End-of-study questionnaire for SPIT. It will ask you a number of questions about how you have tested for HIV in the last 12 months that you have been enrolled in the study. The questionnaire will also ask you some questions regarding your sexual health and your sexual behaviour in the last 12 months and finally, your experiences and impression using the home-based self-sampling HIV saliva testing as a means for testing for HIV.

Please do not be offended if some of the questions seem strange or inappropriate to you. They are of great importance to our study and for this reason the more questions you answer the more valuable the information you provide is for our analysis. If however you do not wish to answer specific questions, please leave them blank.

All information collected from this questionnaire is strictly confidential, will not be traced back to you and will be kept separately from your medical records.

A: Your HIV testing during your time on the study

1. How many times have you tested for HIV in the 12 months of the study (please give as accurate a number as possible)?

   _____

2. In the last year (during the study), **HOW** have you tested for HIV?

Saliva testing only ☐

Saliva testing and blood ☐

Blood tests only ☐

I have not tested for HIV in the last 12 months ☐

B: Your sexual behaviour in the last 12 months sexual health history

3. How many male sexual partners have you had sexual contact with in the last 12 months?

_____

4. How many male sexual partners have you had **UNPROTECTED** anal sex with in the last **12 months**?

_____

5. How many male sexual partners have you had **UNPROTECTED** anal sex with in the last **3 months**?

_____

6. Have you **ever** had a sexually transmitted infection? Yes ☐ No ☐

7. Have you had a sexually transmitted infection during the study 12 months?

   Yes ☐ No ☐

C: Practicalities of saliva testing

8. How easy did you find it to take a sample?

   1 2 3 4 5

   Very Easy Very Difficult

9. Were the instructions to take a sample clear?

   Yes ☐ No ☐

10. Did you have any samples that were inconclusive or inadequate?

    Yes* ☐ No ☐

    *If YES did this worry you enough to stop saliva testing or did you take further tests afterwards?

- I went on to use saliva tests again ☐
- I did not want to use the saliva test again ☐
- I have not tested since using a saliva test but would be happy to do this in the future ☐

11. Did you get a result (negative, positive, inconclusive or inadequate sample) for every test that you sent in?

    Yes ☐ No ☐

12. If saliva testing at home was possible in the future how likely would you be to use this option?

    1 2 3 4 5

Definitely NOT Definitely WOULD

13. Would saliva home testing make it easier for you to test in future?

    Yes ☐ No ☐ Don't know ☐

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

We would like to perform a number of research interviews to discuss your experiences of HIV testing using home saliva testing. Would you be happy to be interviewed at a time which is convenient to you?

Yes, please contact me on _____

Many thanks for taking the time to complete this survey. Please return it as soon as you can to rahma.elmahdi@imperial.nhs.uk

Appendix R: SPIT (Salivary Initiated Patient Testing for HIV) Study Protocol

Written by Dr Sarah Fidler and Dr Alan Winston

SPIT Study: Saliva patient initiated testing for HIV

Feasibility and acceptability of repeat home-based HIV saliva testing using self-sampling amongst men who have sex with

men

Chief Investigator:

Dr Sarah Fidler

Senior Lecturer/Honorary Consultant Physician

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W2 1NY

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Email: s.fidler@imperial.ac.uk

Imperial College NHS Trust

St Mary's Hospital

Street

London

W2 1NY

Tel: 0203 312 6845

Fax: 0203 312 6645

Email: alan.smith@imperial.nhs.uk

Co-Investigator:

Dr Alan Smith

Consultant Physician GUM/HIV

Sponsor:

Ms Lucy Parker

Research Governance Manager , Regulatory Compliance

Imperial College London and Imperial College Healthcare NHS Trust

Room 510A

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Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

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Summary of study

Of the estimated 86500 people living with HIV in the UK; 43% are amongst men-who-have-sex-with-men (MSM) [HPA 2010] and the number of new infections amongst this group continues to increase. Individuals with recently acquired infection disproportionately contribute towards onward transmission in certain groups with high rates of partner change [Hollingsworth Fraser]. Undiagnosed HIV infection levels in MSM remain high in spite of increased access to and promotion of HIV testing in medical and community settings. Approximately 30% of HIV infected MSM remain unaware of their HIV status. Without novel approaches to simplify access to regular testing it seems unlikely that this will significantly change. Previous anonymous saliva based testing has been used in studies to estimate HIV prevalence of MSM in non-hospital settings. We propose using saliva based HIV testing to facilitate self-initiated testing by MSM at home following recruitment in a clinic setting when information about HIV prevention and testing will be given. Frequent HIV testing of MSM is recommended in HIV testing guidelines [BASHH]. Currently a lack of home testing options mean that inconvenience of attending testing services may be a barrier to frequent testing.

The number of cases of new HIV infections amongst MSM continues to increase and the frequency of HIV testing amongst high risk groups within this population remains too low to significantly alter the 30% who remain unaware of their HIV status. One of the key barriers to uptake of HIV testing remains the inconvenience of needing to repeatedly attend health care facilities. There has been a marked improvement in patient HIV testing experiences following the introduction of the point of care technology but this still requires by law attendance with a health care professional in order to deliver results.

Hypothesis:

We propose that self-sampling with oral saliva collection may increase the rate of repeat HIV testing amongst MSM attending a walk-in GUM outpatient service

Abstract:

This is a prospective observational study that will determine the frequency of repeat HIV testing amongst targeted high risk groups compared with their own previous reported testing frequency using current practise. We propose to undertake a pilot feasibility and acceptability of self oral swab HIV-sampling

comparing the frequency of repeat testing using the self-swab sampling technology compared with reported frequency of HIV testing in the preceding 12 month period for that same individual.

The goal of this study is to determine if self-swab sample collection avoiding the need for clinical attendance will increase the frequency of repeat HIV testing amongst high risk MSM populations attending targeted GUM clinical service –the GUYS clinic at St Mary's Hospital.

Setting:

The Jefferiss Wing at St Mary's Hospital is a large central London teaching clinic with over 50 000 GUM visits annually. The on-site HIV clinic has over 2800 regular attendees, with approximately 600 of these not currently requiring treatment. 10 to 20 new diagnoses are made per month, mostly through the GUM clinic but also in hospital inpatients across ICHNT. The majority of recent infections are amongst the younger MSM populations and repeat HIV testing is critical to avoid missed new infections.

The GUYS@ Marys clinic is a dedicated service for younger men who have sex with men. It sees men aged up to 35 years old for comprehensive sexual health screening including HIV testing. There are approximately 800 attendances per year to a late evening clinic. The clinic has a good track record for recruitment to HIV testing studies. HIV testing rates are high. In a patient survey many patients reported choosing this clinic because of its hours as they were unable to attend many clinics due to their work hours. Aim:

To compare the frequency of repeat HIV testing amongst individuals who self-test compared with their reported previous testing behaviour in the preceding 12 month period

To assess the feasibility and acceptability of self-sampling to this population (questionnaires)

Objectives:

To compare the impact of home based saliva testing on frequency of testing compared with reported testing frequency in the preceding 12 month period.

To evaluate the feasibility and acceptability of repeat HIV testing if offered as home-based oral swab collection through a completed self-assessment questionnaire.

Barriers to testing for Human immunodeficiency virus infection in the United Kingdom

Current barriers to repeat HIV testing will be addressed through participant questionnaires. To examine any impact on reported sexual behaviour before and after study enrolment through sexual behaviour questionnaires

Outcome measures:

Primary outcome measure

To compare the number of repeat HIV tests reported for the preceding 12 month period before enrolment into the study compared with number of repeat HIV tests undertaken either through oral swab sampling or clinic attendance over the 12 month study period.

Secondary Outcome measure

To describe the participant experiences of delivering repeat self-sampling for HIV testing

Eligibility criteria:

Age 18 years or older

Able to give written informed consent

Testing HIV negative using standard HIV testing practice at enrolment and willing to enrol into the study

Expects to be UK based for the duration of the study and able to attend the 12 month study visit

Exclusion criteria:

HIV infected at enrolment or symptoms suggestive of seroconversion

Individuals not felt by research clinical practitioners to be appropriate for enrolment based on mental health issues, capacity, ability to give informed consent or high levels of anxiety around HIV

Analysis plan:

Data from HIV testing frequency will be undertaken from patient records as well as self-reported test frequency.

Data from repeat HIV test frequency will be evaluated when the final study participant has completed a 12 month follow up period.

In total 50 participants will be followed up for a total of 12 months, where enrolment will be completed by 6 months after study initiation.

Study Design and Methods:

MSM attending the GUYS clinic who are eligible to join the study will be invited to participate and a participant information sheet will be given.

Standard clinical practice will be followed which will include: STI screen, HIV testing. For those consenting to join the study clinical supervision and written instructions will be given to the participants on how to take an oral swab sample. The venous blood drawn as part of standard care will be stored in the laboratory for potential future testing if required. A baseline study questionnaire will be completed by each consenting participant documenting I formation about previous 12 months HIV testing frequency, sexual behaviour and attitudes towards HIV testing. All information and sampling will be anonymised with a unique number.

A CRF will be completed with the necessary study procedures documented and the frequency and site of HIV testing in the preceding 12 month period will be entered.

A pack containing 6 Self swab sampling kits will be given to all eligible consenting participants.

A final study visit will be arranged for 12 months after enrolment when participants will undergo a repeat full STI screen HIV testing and completion of final study questionnaire.

Participants wishing to access GUM services can attend at any time during the study period.

Results of the individual oral swab testing will be available according to the flow diagram.

Study design

N=50

Eligible participant given patient information sheet

Consent obtained to enrol into study

Baseline STI screen, HIV test questionnaire, Oral swab instructions and specimen collection training

Venous blood sample stored

Provision of 6 home sampling kits with instructions

Whenever participant chooses to repeat test over subsequent 12 month period:

Sample taken and Posted to PO Box address

Results given via participant led choice of following options: a) text, b) email, c) attend clinic, d) letter, e) telephone

Final study visit at 12 months after enrolment

Completion of STI screen HIV testing, end of study questionnaire

Primary study end point:

Frequency of repeat HIV testing using self swab sampling compared with preceding reported HIV-testing frequency

Participants will be given 6 separate HIV oral swab kits in 6 separate stamp addressed envelopes to be posted back to a PO Box address. A unique anonymised ID number will be allocated to each sample with date of birth. Research staff will regularly empty the PO Box and all samples will be sent through internal sample processes currently in place to the diagnostic virology laboratory. Participants will be asked to confirm their preferred method of receiving results (by attending the clinic, by text, telephone, letter or by email) and confirming their mobile phone / contact details. No patient names of addresses will be on any of the samples or request forms.

For participants requiring more swabs a direct request can be made of the research team who can make them available for the participant to collect from the clinic.

Results:

Results of the oral swab tests will take maximum of 2 weeks to be available to the study participants. The laboratory will log the receipt of the oral swab samples which will automatically alert the clinical results teams. A text message will be sent to the study participant confirming receipt of their recent swab and requesting confirmation of preference for receipt of result from the following options:

Text message/email/ telephone/ attendance at clinic/letter

Once results are available the participant will be informed of their results via the stated preferred method

No results will be available outside of clinic opening hours to ensure that any potential HIV+ test results can be dealt with immediately by appropriately trained staff. Any participant testing HIV+ not known to receive their result will be followed up with the research team in conjunction with the standard clinical procedures for patients who need to be informed of a potentially HIV positive, an equivocal result or where testing is not possible and needs a further sample. No HIV+ test result will be given outside of clinic contact, in the case of an equivocal test of positive test result the participant will be invited to re-attend the clinic urgently for repeat blood testing to confirm HIV status.

Participant questionnaires

Feasibility and acceptability of the testing strategy will be evaluated through participant specific questionnaires that are administered at enrolment and final study visit 12 months later.

Ethics approval

The Chief Investigator has obtained approval from the Research Ethics Committee (12/LO/0556). The study must be submitted for Site Specific Assessment (SSA) at each participating NHS Trust. The Chief Investigator will require a copy of the Trust R&D approval letter before accepting participants into the study. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

Consent

Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet offered and time allowed for consideration. Signed participant consent should be obtained. The right of the participant to refuse to participate without giving reasons must be respected. After the participant has entered the study the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so should be recorded. In these cases the participants remain within the study for the purposes of follow-up and data analysis. All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

Confidentiality

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

Indemnity

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

Sponsor

Imperial College Academic Health Science Centre will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

Funding

The British HIV Association (BHIVA) is funding this study. The amount of funding is £7000

Audits

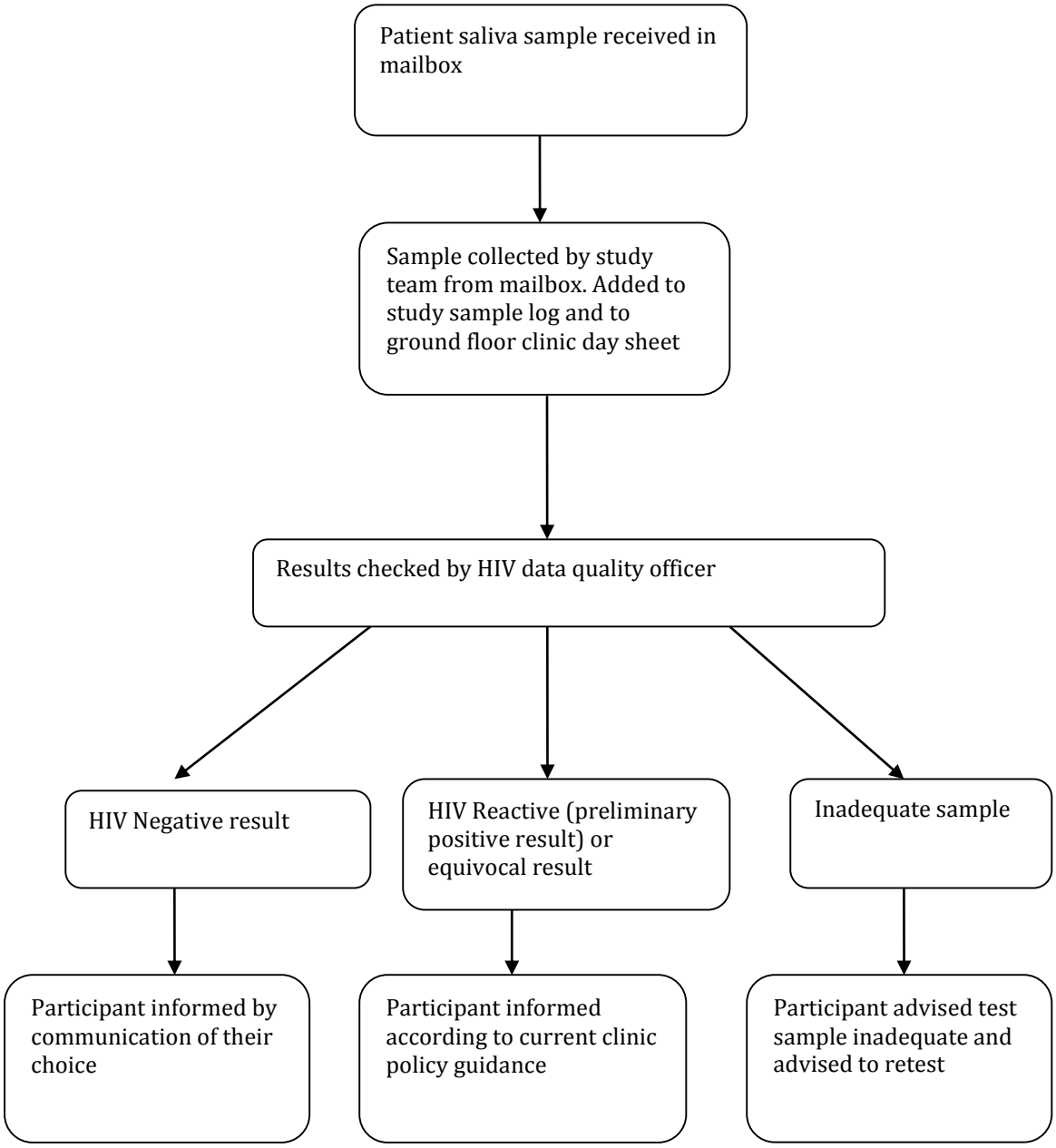
The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

Study Management

The day-to-day management of the study will be co-ordinated through the Clinical Trials Centre.

Publication Policy

[The study's publication policy should be described in full]


Patient saliva sample received in mailbox
Sample collected by study team from mailbox. Added to study sample log and to ground floor clinic day sheet
Results checked by HIV data quality officer
HIV Negative result
HIV Reactive (preliminary positive result) or equivocal result
Inadequate sample
Participant informed by communication of their choice
Participant informed according to current clinic policy guidance
Participant advised test sample inadequate and advised to retest

Appendix S: SPIT Topic Guide for semi-structured interviews

Patient In-depth interview Topic Guide

Study Title: SPIT Study: Saliva patient initiated testing for HIV

Feasibility and acceptability of repeat home-based HIV saliva testing using self-sampling amongst men who have sex with men

Chief Investigator Dr Sarah Fidler

Ethics Ref: 12/LO/0556

Before the interview

Request permission to record the interview and show the patient the device.

Explain why the interview is being recorded and that the recording will not be heard by anyone except the investigator and the person transcribing the audio recording.

Reassure the patient that everything discussed will remain confidential.

Request that the respondent is honest when answering the questions and that they attempt to answer the interview questions as fully as possible.

Explain that the purpose of the interview is to develop an idea of how the patient has found the experience of using the self-sample swabs for HIV testing in the last year, how that may have had an impact on their risk taking and other ways for testing for HIV.

Explain that you will not be taking written notes, however you will be making a written copy of the recording for later analysis. This copy will be anonymised with only a study number with no identifiable details.

Clarify that if there is any subject the patient is uncomfortable talking about then they should not feel obliged to do so and that they can stop at any point should they wish to take a break or stop the interview.

Check that the patient is comfortable with this and wishes to continue.

Clearly signpost the different topic areas being covered and summarise what the patient has said periodically during the course of the interview.

Tell the patient that you are going to be asking them to reflect in some depth on points that they might not have given a great deal of consideration to in the last year, such as their ideas on use of the swab. Ask them to take their time in answering these questions. Explain that there is no rush as we are keen to get a complete account of their experiences.

Ask if they have any further questions regarding any of the above?

Topics to cover

Experience using the self-sampling swabs

Sexual experiences in the last 12 months

HIV testing practice in the last 12 months

Views on HIV testing options available

Experience using the self-sampling swabs

How often have you tested using the swabs?

How did you find using the swabs?

If you did use the swabs why did you use them and if not, why did you not to use them?

What part, if any, did having the swab play in the type of sexual risks you had in the last year?

Sexual experiences in the last 12 months

Can you tell me about your sexual relationships in the last year?

How could you classify the kind of sex you've had in the last year in terms of risk?

How would you describe the difference between 'risky sex' and 'safe sex' for you?

How has this played a part, if any, on your overall testing for HIV in the last year?

HIV testing practice in the last 12 months

How else did you choose to test for HIV in the last year?

For every occasion where you've tested for HIV in the last year, can you tell me where you went to receive the test, why you chose to test and your experience testing on that occasion?

How were the other ways you chose to test from HIV different from using the self-sampling swab?

What were the benefits or problems in these differences in testing for you personally?

How is testing for HIV important for you in maintaining your general health?

Your views on HIV testing options available to you

How do you feel about the choice for HIV testing available to you?

Do you feel you are aware of all ways that you can choose to test for HIV?

Do you believe that these options suit you and your lifestyle?

How would you like to test for HIV in the future?

Summary

Is there anything we haven't discussed that you'd like to mention?

What do you think have been the most important points that we've touched on during this interview?

Would you like to elaborate on any of this further?

Appendix T: Complete Stata code for SPIT Quantitative data analysis

```
import excel "C:\Users\Rahma Elmahdi\Desktop\spit41.xlsx", sheet("Sheet1")
```

```
gen studydurationdays = recalldate-recruitdate

gen studyduration = studydurationdays/365.2

sum studyduration

tab ntestyear

sum studyduration, d

tab swabno

sum swab1date

sum swab2date

sum swab3date

sum swab4date

tab swabno

tab easesample

sum sex3month, d

tab nsti

sum studyduration

tab testhow

tab swabno

tab ntestyear

tab sex3months

tab nstiyear

tab startnstiyear
```

ttest nstiyear==startnstiyear

lab define nstiyear 0"no" 1"yes"

lab values nstiyear nstiyear

tab nstiyear ntestyear

tab ntest nsti

lab define nsti 0"no" 1"year"

lab values nstiyear nstiyear

tab nstiyear ntestyear

lab values nstiyear nstiyear

tab nstiyear ntestyear

xi logistic nstiyear i.ntestyear

logistic nstiyear i.ntestyear, or

regress nstiyear ntestyear

regress nstiyear ntestyear, robust

xi: logistic nstiyear i.ntestyear, or

logit nstiyear ntestyear, or

tab ntestyear if nstiyear ==1

tab ntestyear if nstiyear == 0

ranksum ntestyear, by (nstiyear)

tab ntestyear nstiyear

tab sex3months

```
sum sex3months, d

sum startnsex3months, d

ttest sex3months==startnsex3months

regress sex3months ntestyear

gen HIVtest = ntestyear

replace HIVtest =0 if ntestyear <2

replace HIVtest = 1 if ntestyear >1

lab define HIVtest 0"1 test" 1">1 test"

lab values HIVtest HIVtest

xi: logistic nstiyear i.HIVtest

xi: logistic nstiyear i.HIVtest, or

xi: logistic sex3months i.HIVtest, or

tab sex3months

ttest HIVtest, by (nstiyear)

tab ntestyear if testhow == 1

tab ntestyear if testhow == 2

tab nstiyear if ntestyear==0

tab sex3month if ntestyear == 0

tab unsex3month if ntestyear ==0

tab sexyear if ntestyear==0

tab unsexyear if ntestyear ==0
```

```
gen duration1 = swab2date - swab1date

tab duration1

gen duration = swab1date - recruitdate

tab duration

gen swabtime = duration/365.2

tab swabtime

sum duration, d

sum duration

drop swabtime

gen swabtime = duration/7

tab swabtime

replace swabtime = 0 if duration >125.2

replace swabtime = 1 if duration <125.2

tab swabtime

replace swabtime = . if swabno == 0

tab swabtime

tab swabno

replace swabtime = . if swabno <1

tab swabtime

replace swabtime = 1 if duration >125.2

replace swabtime = 2 if duration < 125.2
```

```
replace swabtime = 0 if swabno <1

tab swabtime

replace swabtime = 0 if duration <358

replace swabtime = 1 if duration <125.2

tab swabtime

replace swabtime = . if duration <1

tab swabtime

regress duration ntest

regress duration nstiyear

xi: logistic swabtime i.nstiyear, or

tab duration1

sum duration1

sum duration1, d

gen swabrisk = swabno

replace swabrisk = . if swabno == 0

replace swabrisk = 0 if swabno == 1

replace swabrisk = 1 if swabno ==2

replace swabrisk = 1 if swabno == 3

replace swabrisk = 1 if swabno == 4

tab swabrisk

xi: logistic nstiyear i.swabrisk, or
```

```
xi: logistic swabrisk i.nstiyear, or

tab swabrisk nstiyear

tab swabrisk

tab ntestyear if nstiyear == 1

ttest ntestyear, by (nstiyear)

ttest sex3months, by(swabrisk)

gen testrisk = ntestyear

replace testrisk = . if ntestyear ==0

replace testrisk = 0 if ntestyear == 1

replace testrisk = 1 if ntestyear >1

replace testrisk =. if ntestyear == 0

replace testrisk = . if ntestyear == 0

tab testrisk

tab testrisk if ntestyear == 1

sum ntestyear

replace testrisk = 1 if ntestyear <7

tab testrisk

tab testrisk

replace testrisk = 0 if ntestyear <2

tab testrisk

replace testrisk = . if ntestyear == 0
```

```
tab testrisk

xi: logistic testrisk i.nstiyear, or

drop testrisk

gen testrisk = .

replace testrisk = 0 if ntestyear == 1

replace testrisk = 1 if ntestyear == 2

replace testrisk = 1 if ntestyear == 3

replace testrisk = 1 if ntestyear == 4

replace testrisk = 1 if ntestyear == 5

replace testrisk = 1 if ntestyear == 6

tab testrisk

xi: logistic testrisk i.nstiyear, or

replace testrisk = 0 if ntestyear == 0

tab testrisk

xi: logistic testrisk i.nstiyear, or

xi: logistic testrisk i.sex3months, or

tab testrisk nstiyear

tab nchlayear

tab nsyphyear

tab ngonyear

tab sexhiv
```

```
tab ntestyear if sexhiv == 1

tab nstiyear if sexhiv == 1

tab sex3months if sexhiv == 1

xi: logistic testrisk i.sexhiv, or

xi: logistic sexhiv i.testrisk, or

tab easesample

tab instructsample

tab resultsample

tab easehome

log close
```

Acknowledgements

I would like to express my special appreciation and thanks to my supervisor Professor Helen Ward who has been a great mentor for me during my time researching for this thesis and an inspiration to me for many years before that. I would like to thank her for encouraging my research and allowing me to grow in confidence not only as a researcher but also as a person. I would also like to thank my supervisors Dr Graham Cooke and Dr Sarah Fidler for sharing their knowledge on the realities of being a research scientist and having a clinical career and showing me, through their own work, that it is possible to be a great success in both. A special thanks is also due to the academic staff in our department in particular, Dr Sarah Gerver and Dr Gabriela Gomez Guillen for not only supporting me in the development of analytical skills essential for my research but also for having enough faith to commit to co-authoring a piece of work with me. Many others have also played a part in the development of my research skills, particularly Dr Tanvi Rai and Dr Juan Gonzalez-Maffe who are proof to me that your greatest teachers can also become your good friends.

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