



National Public Health Monitoring of Incident HIV-1 Infections and Primary Drug Resistance

Clinic Protocol

Health Protection Agency

Centre for Infections

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1. Background

In the UK, since the first cases of HIV were reported in mid-1982, there have been over 88,000 individuals reported to the Health Protection Agency, of whom 52,000 are accessing HIV-related care services. Estimates to include those with undiagnosed infections, among 15-59 year olds, suggest that in 2006 around 73,000 individuals were living with HIV in the UK. Newly diagnosed cases of HIV have been increasing since the mid 1990s. This increase has been fuelled in part by an increase in heterosexually acquired infections among migrant populations, most of whom acquired their infection in sub-Saharan Africa as well as among men who have sex with men (MSM), the majority of whom acquired their infections within the UK.

The public health monitoring of HIV poses unique challenges as a result of the extended period between infection and the onset of symptoms, which is typically between eight and eleven years. Current diagnostic tests for HIV are unable to distinguish recently acquired infections (incident infections) from long standing infections. As a result, we have no way of directly assessing whether the increase in the number of newly diagnosed infections in the UK is as a result of the success in promoting HIV testing, or a failure to reduce HIV transmission.

Recent laboratory advances, however, have made it possible to identify infections that are likely to have been acquired within a well defined recent time frame, which can be used as a basis for determining the incidence of infection as a key indicator of HIV transmission. The generic term 'Recent Infection Testing Algorithm' (RITA) has been coined to embrace the several serological methods that have been described to distinguish a recent infection. In the UK, RITA has been applied on a small scale within the unlinked anonymous sentinel serosurveillance of sexually transmitted infections among clinic attendees in England. This has enabled HIV incidence in MSM to be measured since the early 1990s*. However, this information is limited to those MSM attending the 16 participating clinics.

2. Rational

The HPA is establishing HIV incidence surveillance as an extension to the current HIV surveillance system established in the mid-1980s. Our intention is to better characterise the HIV epidemic by identifying populations and/or subpopulations where a greater risk of

* Murphy G *et al.* HIV incidence appears constant in men who have sex with men despite widespread use of effective antiretroviral therapy. *AIDS*. 2004;18(2):265-

transmission, and therefore a greater need for intervention exists. Estimates of HIV incidence can also supply additional information for advocating, designing and planning public health action as well as providing a direct means for evaluating the impact of intervention initiatives. To meet these objectives, we intend, through a phased roll-out, to include RITA testing for all newly diagnosed cases of HIV to identify all recently infected cases.

3. Aims

Working in close collaboration with national and local laboratory and GUM services, the aims of the Public Health Monitoring of Incident HIV-1 Infections and Primary Drug Resistance are to:

Locally:

- Provide the proportion of local infections that are likely to be recent.
- Provide links between resistance and incidence results for the local monitoring of primary drug resistance.
- Provide data to inform and evaluate local health promotion and HIV prevention initiatives.

Nationally:

- Provide the proportion of national infections that are likely to be recent.
- Provide appropriately stratified national estimates of HIV incidence.
- Integrate the national database of newly diagnosed HIV infections with the MRC HIV resistance database for the national monitoring of primary drug resistance.
- Provide data to inform and evaluate national health promotion and HIV prevention initiatives

4. Design and Implementation

i. Overview

All newly diagnosed HIV infections within the UK are routinely reported to the Centre for Infections at the HPA. Through a phased roll-out, it is intended that at RITA test will be performed on all newly diagnosed cases in the UK. Left over diagnostic sera, blood or plasma from all newly diagnosed cases, that satisfy the inclusion criteria, will be sent from the diagnostic laboratory, in accordance with the local transportation and shipping guidelines, to the Virus Reference Department at the HPA, for RITA testing.

RITA test results will be linked to the routinely collected HIV surveillance reports for each individual and returned to each clinic and diagnostic laboratory within 2 weeks. It will be the prerogative of the clinician and the clinical team to reconcile the results of the RITA assay with the individual patient's notes and return the test results to the patient.

In addition, a HIV Incidence Advisory Group, composed of HIV epidemiologists, virologists and clinicians, along with representatives from BHIVA, BASHH, SSHA, Terrence Higgins Trust, the National African HIV Prevention Programme and the African HIV Policy Network, has been set up to oversee the implementation of the surveillance initiative.

ii. Patient Information Sheet

A short patient information sheet has been compiled and may be used to give each newly diagnosed patient some general information about the routine tests carried out following a positive HIV diagnoses. The tests mentioned include CD4 counts, viral loads and HIV resistance tests as well as the additional HIV incidence (RITA) test. Clinicians, nurses and sexual health advisors should give each patient the opportunity to discuss RITA testing in the context of the other tests used to better characterise their infection, and allow the patient ample opportunity to decline any of the tests offered. Individual centres, however, may have their own information sheet that can be modified to include RITA testing.

iii. The Sample

An aliquot of serum or plasma from all confirmed HIV positive samples should be sent to the Virus Reference Division, at the Health Protection Agency (HPA), Colindale, for RITA testing. Requests for RITA tests can be made using the HIV test request form (see section 11) which captures the information necessary to link the RITA test result for the national surveillance data. RITA test requests can be accepted in other formats, providing that key data fields are provide to allow the results of the RITA test to be linked with the national surveillance data. RITA testing will be offered at no additional charge, providing that the cost of transporting samples to the HPA, Colindale, can be absorbed by the collaborating laboratory.

iv. Eligibility criteria:

Specimens should be submitted where the following conditions are satisfied:

- Confirmed to be anti-HIV-1 antibody positive;
- First HIV diagnosis
- Over 16 years old;

- Total sample volume available for submission is >0.5mls, although samples in excess of 0.2mls can still be submitted, but will allow only minimal testing.

v. Epidemiological Information

All necessary epidemiological information will be collected through the existing routine HIV surveillance forms received at the HPA Centre for Infections. Samples sent from the diagnostic laboratory for RITA testing using the HIV test request form (see section 11) or any other agreed format, will include a combination of the individuals locally assigned clinic number, date of birth, soundexed surname. This information will enable the results of the RITA test to be linked to our existing routine surveillance. Please ensure that sufficient patient information is made available to the laboratory when requesting a HIV test to ensure that the laboratory can provide us with information where necessary.

vi. Linking Recent Infections to New Diagnoses and the UK Resistance Database

All newly diagnosed HIV infections within the UK are routinely reported to the Health Protection Agency (HPA), and in line with the British HIV Association (BHIVA) guidelines, all new diagnoses are recommended to be accompanied by a resistance test. The collection of patient identifiers will enable the results of the RITA test to be accurately linked with the national databases containing the epidemiological information supplied by the clinic for each new diagnosis, and the associated resistance tests. This level of linkage will form the foundation for incidence and primary drug resistance monitoring at the local and national level.

vii. RITA Testing Retrospective Samples

Our intention is to extend RITA testing to stored diagnostic material from HIV diagnoses made between 1st January 2005 and the date at which each centre enrolls in the collaboration. This will enable data from the prospective service to be compared to data for previous years, and provide immediate information on the trends in HIV incidence. We will also be able to more rigorously address additional issues such as the representativeness and biases in the retrospective study outcomes. Retrospective RITA test results will be returned to their originating clinic using the same mechanism as the proposed prospective programme.

5. Caveats and Considerations

Although tests for HIV incidence have been extensively validated and perform well, several factors may affect their performance. As a result, practically, they can only give an approximate indication of recent seroconversion. Factors which can have an affect the sensitivity and specificity of these tests include advanced disease, HAART and infection with subtypes other than B as well as medical conditions such as hyper- or hypo-gammaglobulinemia. Thus, results indicative of a recent seroconversion must be interpreted with care and always in the context of an individual's clinical data.

We will be seeking feedback from the clinic on any medical condition that may affect the serological testing methodologies where the patient has taken anti-retrovirals within 6 months of their diagnosis, and on instances where the clinical data suggests a non-recent infection. Comments can be included in the 'Comment' section of the buff-coloured 'HIV, AIDS or Death Report Form' used to report all new cases of HIV.

6. Conformity with the Human Tissue Act

All diagnostic samples received by the HPA will be accompanied by only minimal data equivalent to a subset of that already collected for each newly diagnosed individual in the UK. Data is collected to allow linkage to existing databases for the purpose of local and national public health monitoring, and informing public health action.

7. Conformity with Confidentiality and Caldicott

Appropriate registration is in place for the handling of all data associated with this project, full details of which are available upon request ^{†‡§}.

[†]The HPA is registered under the [Data Protection Act 1998](#) (registration number Z7749250) to handle data for diagnostic, public health and other purposes. The Agency is very careful to maintain its procedures strictly within the requirements of the DPA.

[‡] The HPA is also registered under Section 60 of the [Health and Social Care Act 2001](#) and has approval from the Patient Information Advisory Group (PIAG) to handle data for purposes that include surveillance and the control of disease, even where specific patient consent has not been given.

[§] Statutory Instrument 2002 No. 1438 in [The Health Service \(Control of Patient Information\) Regulations 2002](#) provides the legal basis for this data handling. It is included on the HPA website and may also be found at

8. Ethical Considerations

The Public Health Monitoring of Incident HIV-1 Infections and Primary Drug Resistance is an extension of the HIV and AIDS surveillance system established in the mid-1980s for all new diagnoses of HIV and AIDS. However, to address any possible ethical concerns that may arise during the implementation of HIV incidence monitoring, we have applied for, and received SSA exempt NHS Research Ethics Committee (MREC) approval.

9. Outputs

i. Reporting recent HIV infections

Results of the RITA test are intended to be returned directly to the requesting laboratory and clinic within two weeks of receiving the batched samples. Reports will be made at the individual patient level, identified by the requesting laboratory ID number.

ii. Additional Reports

Regular outputs from the UK incidence project are intended to be circulated to all collaborating laboratories and clinics and will include:

- Biannual HIV incidence newsletters
- National and regional HIV incidence surveillance tables
- HIV/STI annual reports
- Conference presentations and abstracts
- Peer reviewed publications

10. Overview



