

**HIDES – (HIV Indicator Diseases across Europe Study)
Survey Protocol**

Version: 1.1 (11 November 2011)

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Differs from version 1.0 (19 June 2009) with the addition of the following indicator diseases/conditions :

- Presenting with pneumonia, admitted to hospital for at least 24h
- Presenting with unexplained lymphadenopathy
- Presenting with peripheral neuropathy of unknown cause (diagnosed by neurologist)
- Presenting with primary lung cancer
- Presenting with severe or recalcitrant psoriasis (newly diagnosed)

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HIV Indicator Diseases Survey

I. Background:

Most patients infected with HIV across the European continent remain undiagnosed; although this percentage varies markedly from 15-80% across the continent. Undiagnosed HIV is harmful to the person infected as appropriate health interventions are then delayed until the HIV infection is diagnosed. It is also detrimental to society as persons unaware of their HIV infection may transmit more frequently to others than persons that are aware of their HIV status.

An important public health issue is hence how to diagnose more HIV-infected persons earlier in the course of their infection. In the US, the Centres for Disease Control and Prevention (CDC) have introduced testing guidelines where all persons are tested upon entry into the hospital system (the “opt-out” testing guidelines).

At the “HIV in Europe” conference held in November 2007, the general sense was that such an approach would not be suitable for Europe. Conversely, the conference recommended further development of focused HIV testing in patients presenting with certain clinical conditions and/or diseases (i.e. indicator condition guided testing).

Cost effectiveness analyses suggests cost savings if a population with a HIV prevalence of 1% or more are tested although this rate may be as low as 0.1%. However, there is very little – if any - evidence on HIV prevalence for various conditions and diseases in specific and easy to identify sections of society. This is true in general and particularly across the European continent.

II. Aim:

Implement a survey initiative to assess HIV prevalence for one or more diseases and/or conditions within a specific segment of the population not yet diagnosed with HIV and that present for care with the specific disease/condition.

The implementation will be conducted in two phases. Protocol version 1.0 implemented surveys in 8 diseases associated with high-risk behaviour or immune deficiency. Protocol version 1.1 will implement surveys of 11 diseases/conditions (listed below).

A. List of Indicator Diseases

The list of diseases below is not indicative of the most important indicator diseases for HIV but rather a list of diseases suggested for surveillance.

During protocol version 1.0, a total of 3588 patients were enrolled. Protocol version 1.1 will enrol patients presenting with the following diseases/conditions:

1. Presenting for care of malignant lymphoma, irrespective of type
2. Presenting for care of cervical or anal dysplasia or cancer, (Cervical CIN II and above)
3. Presenting for care of Hepatitis B or C virus infection (acute or chronic – and irrespective of time of diagnosis relative to time of survey),
4. Presenting with ongoing mononucleosis-like illness
5. Presenting with unexplained leukocytopenia or thrombocytopenia lasting at least 4 weeks
6. Presenting with seborrheic dermatitis / exanthema

7. Presenting with pneumonia, admitted to hospital for at least 24h
8. Presenting with unexplained lymphadenopathy
9. Presenting with peripheral neuropathy of unknown cause (diagnosed by neurologist)
10. Presenting with primary lung cancer
11. Presenting with severe or recalcitrant psoriasis (newly diagnosed)

B. Procedures:

Aims of the survey: One survey assesses HIV prevalence for one specific disease/condition for a specific segment of the population within a specific setting (see Aim above for diseases to be studied). The setting can perform more than one survey on other diseases or conditions. For example, a clinic might be able to do one survey with patients presenting with a primary lung cancer and one survey with patients presenting with malignant lymphoma.

C. Conduct of the survey:

Each survey should be implemented within a segment of the population that is logical, specific, and easy to identify, and within a specific setting (e.g. an emergency section a hospital, a department that receives an unselected number of persons with a given disease/condition of interest, a general practitioner, a dentist or a dermatologist). The survey will be implemented on consecutive patients not yet known to be HIV-infected and that present with only one of the 11 conditions mentioned above from a given day until a pre-specified number of persons have entered the survey (at least 100 patients but preferentially 200-400 being tested for HIV).

III. Ethical approvals

Appropriate local and national ethical approvals will need to be obtained. For each person entering the survey, an informed consent is obtained according to the local and national regulations for where the survey is being conducted. The person conducting the survey is responsible for ensuring these approvals are in place and for those accepting an HIV test, that this test is performed. Persons participating in the survey will be informed of the result of their test and referred to appropriate treatment and counselling centres. Those patients informed of a positive test result will be referred to a HIV clinician.

IV. Data Collection

Variables from the survey at a minimum should include the disease/condition surveyed, age, gender, whether the patient has accepted an HIV test, and the result of the HIV test. This information will be collected at the centre and should be sent to the coordinating centre. There will be a possibility to submit this electronically in an online format or via fax or email.

Persons performing a survey are encouraged to collect and report more detailed analyses and the provision of a more detailed description of the population entering the survey (e.g. co-morbidity, ethnicity, sexual preference; prior and/or current use of injection of illicit drugs; prior and/or current history of sexually transmitted diseases; prior and/or current history of hepatitis B and C virus infection) would be most welcome (specific additional sections of the online service will be developed for the submission of such information). This information will only be collected for patients with positive HIV test results.

A. Alternate approach for the conduct of a survey:

Retrospective implementation is also a possibility if blood is available from a segment of the population for one or more diseases/conditions in at least 100 consecutive persons within a specific

setting presenting with one or more diseases/conditions, and ethical clearance can be obtained from the ethical review board to perform an anonymous testing of these samples, this can be conducted as an alternative to the survey.

B. Submission of data:

Survey data will be collected either by submitted completed paper copies of case-record-forms (CRF) for central data-entry or via an online service that will permit relevant data to be entered by the persons responsible for a given survey for individual persons either prospectively as the survey evolves or once it is completed. Example of format of a “base” CRF and an “extended CRF” is depicted in Appendix I.

V. Ownership of data:

The investigator responsible for completing the survey is the owner of the data and can freely publish the data as she/he see fit. By submitting the data however to the Coordinating Centre, the person responsible for the survey allows for the data to be used in a meta-analysis of the situation across the continent.

A. Who can be responsible for the conduct of the survey?

Those implementing the survey would be health professionals, NGO’s, public health officials, and other professionals depending on the population and the setting where the survey is being conducted.

VI. Incentive for submitting report on survey:

Surveys fulfilling the minimum criteria will be reimbursed, as will costs for HIV tests.

A. Incentive for submitting data to central survey database:

For surveys fulfilling the above mentioned criteria, the survey principal investigator will become part of the survey study group and involved in the analyses and reporting of the results.

B. Membership of the survey study group

The survey study group will be responsible for the meta-analysis of the surveys across the continent. A group with representation from the EACS executive committee (Nathan Clumeck, Antonella d’Arminio Monforte, Jose Gatell, Jens D. Lundgren), from BHIVA (Brian Gazzard), the scientific coordinator of the project, members of HIV in Europe leadership, and all persons responsible for one or more surveys submitted will constitute the study group moving this project forward.

VII. Timelines and evaluation of the project:

The project will be launched in Fall 2011. Surveys completed retrospectively from the beginning of 2010 can be included. The surveys will run for 18 month, whereafter the meta-analyses of the surveys will be conducted for presentation.

Appendix 1: Survey Report Centres

HIDES 2: HIV Indicator Diseases Enrolment		FORM A
Section A. Demography		
A1. Year of Birth (yyyy): _____	A2. Gender: <input type="checkbox"/> male <input type="checkbox"/> female	
A3. Ethnicity <input type="checkbox"/> white <input type="checkbox"/> asian <input type="checkbox"/> black <input type="checkbox"/> unknown		
Section B. Indicator Disease		
Patient presenting with: <i>(based on treating physician's clinical or microbiological diagnosis)</i>		
Please only tick one box in either A,B,C,D,E,F,G, H, I, J, K		
<input type="checkbox"/> A. Malignant lymphoma <i>(Irrespective of type)</i>		
<input type="checkbox"/> B. Cervical or anal dysplasia or cancer <i>(CIN II and above)</i> <input type="checkbox"/> Cervical dysplasia/cancer <input type="checkbox"/> Anal dysplasia <input type="checkbox"/> Anal cancer <input type="checkbox"/> Unspecified		
<input type="checkbox"/> C. Hepatitis B or C virus infection <i>(Acute or chronic – and irrespective of time of diagnosis relative to time of survey)</i> <input type="checkbox"/> Hep B <input type="checkbox"/> Hep C <input type="checkbox"/> Unspecified		
<input type="checkbox"/> D. Ongoing mononucleosis-like illness		
<input type="checkbox"/> E. Unexplained leukocytopenia or thrombocytopenia lasting at least 4 weeks		
<input type="checkbox"/> F. Seborrheic dermatitis / exanthema		
<input type="checkbox"/> G. Pneumonia		
<input type="checkbox"/> H. Unexplained lymphadenopathy		
<input type="checkbox"/> I. Peripheral neuropathy <i>(of unknown cause)</i>		
<input type="checkbox"/> J. Primary lung cancer		
<input type="checkbox"/> K. Severe or recalcitrant psoriasis <i>(newly diagnosed)</i>		
Section C. HIV Test Results		
C1. Previous HIV serological status (patients must <u>not</u> be known to be HIV infected at the time of survey)		
Previously tested for HIV <input type="checkbox"/> yes <input type="checkbox"/> no		
If yes: Most recent previous negative HIV test (dd-mm-yyyy): ____-____-____		
Total number of previous negative tests: _____		
C2. HIV test result: <input type="checkbox"/> positive <input type="checkbox"/> negative Date of blood sample (dd-mm-yyyy): ____-____-____		

C3. Patient received test result: yes no

Completed by (investigator's initials)	Date Completed (dd-mm-yyyy)
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Section A. HIV Infected

CD4 cell counts (closest to diagnosis): value: _____	Date (dd-mm-yyyy): __-__-____
HIV-RNA values: _____ units	Date (dd-mm-yyyy): __-__-____

Section B. Additional Data Items

	<p>B1. Sexual orientation</p> <p><input type="checkbox"/> heterosexual</p> <p><input type="checkbox"/> homosexual</p> <p><input type="checkbox"/> bisexual</p> <p><input type="checkbox"/> unknown</p>				
<p>B2. Active intravenous drug use: <input type="checkbox"/> yes <input type="checkbox"/> no</p>					
<p>B3. Has the patient had any signs of less serious HIV related symptoms within the last 5 years:</p> <p><input type="checkbox"/> Mononucleosis-like illness</p> <p><input type="checkbox"/> Oral candidiasis</p> <p><input type="checkbox"/> Herpes Zoster</p> <p><input type="checkbox"/> Unexplained leukocytopenia or thrombocytopenia</p> <p><input type="checkbox"/> Seborrheic dermatitis / exanthema</p> <p><input type="checkbox"/> None</p>					
<p>B4. Diagnosed sexually transmitted diseases within the last 5 years:</p> <p><input type="checkbox"/> Gonorrhoea</p> <p><input type="checkbox"/> Syphilis</p> <p><input type="checkbox"/> Other ulcerative genital conditions</p> <p><input type="checkbox"/> Chlamydia</p> <p><input type="checkbox"/> Unspecified</p> <p><input type="checkbox"/> None</p>					
<p>B5. Any previous test of HBV: <input type="checkbox"/> yes <input type="checkbox"/> no</p> <p>If yes: Test result: <input type="checkbox"/> positive <input type="checkbox"/> negative When: (dd-mm-year) __-__-____</p>					
<p>B6. Any previous test of HCV: <input type="checkbox"/> yes <input type="checkbox"/> no</p> <p>If yes: Test result: <input type="checkbox"/> positive <input type="checkbox"/> negative When: (dd-mm-year) __-__-____</p>					
<p>B7. Any hospitalization within the last 5 years: <input type="checkbox"/> yes <input type="checkbox"/> no</p> <p>Due to:</p> <p>Severe opportunistic infections (including AIDS defining):</p> <p>Please use codes below or write the full type for any severe opportunistic infection not listed</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Diagnose</td> <td style="width: 70%;">Date of diagnosis (dd-mm-yyyy)</td> </tr> <tr> <td>_____</td> <td>__-__-____</td> </tr> </table>		Diagnose	Date of diagnosis (dd-mm-yyyy)	_____	__-__-____
Diagnose	Date of diagnosis (dd-mm-yyyy)				
_____	__-__-____				

_____	__-__-__
_____	__-__-__

BCNE: Bacterial pneumonia, recurrent (>2 episodes within 1 year)	HIST: Histoplasmosis, extrapulm.	NHLB: Non-Hodgkin lymphoma Burkitt (Classical or Atypical)
CANO: Candidiasis, oesophageal	ISDI: Isosporiasis diarrhoea (duration >1 month)	NHLI: Non-Hodgkin lymphoma Diffuse large B-cell lymphoma (Immunoblastic or Centroblastic)
CMVR: Cytomegalovirus (CMV) chorioretinitis	KS: Kaposi's sarcoma	NHLU: Non-Hodgkin lymphoma Unknown/other histology
CMVO: CMV - other location, specify	LEIS: Leishmaniasis, visceral	NHLP: Non-Hodgkin lymphoma Primary brain lymphoma (at diagnosis, involvement of the central nervous system without other organ affection - regardless of histology)
CRCO: Cryptococcosis, extrapulm.	LEU: Progressive multifocal leucoencephalopathy	PCP: Pneumocystis jiroveci pneumonia (PCP)
CRSP: Cryptosporidiosis (duration > 1 month)	MC: Mycobact. avium complex (MAC) or Kansasii, extrapulm	SAM: Salmonella bacteriaemia (non-typhoid) (>2 episodes)
CRVC: Cervical cancer	MCP: Mycobact. tuberculosis, pulm.	TOX: Toxoplasmosis, brain
FBLS: Focal brain lesion	MCX: Mycobact. tuberculosis, extrapulm.	
HERP: Herpes simplex virus ulcers (duration >1 month) or pneumonitis/esophagitis	MCXO: Mycobact. extrapulm., other type, specify	

Other severe infections/cancers:

Please use codes below or write the full type for any severe infection/cancer not listed

Diagnose	Date of diagnosis (dd-mm-yyyy)
_____	__-__-__
_____	__-__-__
_____	__-__-__

ALL: Acute lymphoid leukemia	ENDO: Endocarditis	MULM: Multiple myeloma
AML: Acute myeloid leukemia	HDL: Hodgkin lymphoma	PENC: Penile cancer
ANUS: Anus cancer	KIDN: Kidney cancer	PERI: Peritonitis
BACT: Bacteremia	LIVR: Liver cancer	PNEU: Pneumonia
BLAD: Bladder cancer	LUNG: Lung cancer	PROS: Prostate cancer
BRCA: Breast cancer	LIPC: Lip cancer	PYEL: Pyelonephritis
CERV: Cervical dysplasia/carcinoma in situ	MALM: Malignant melanoma	OSTI: Ostitis
CLL: Chronic lymphoid leukemia	MEAC: Metastasis of adenocarcinoma	RECT: Rectum cancer
CML: Chronic myeloid leukemia	MENI: Meningitis	STOM: Stomach cancer
COLO: Colon cancer	MEOC: Metastasis of other cancer type	TESE: Testicular seminoma
COTC: Connective tissue cancer	MESC: Metastasis of squamous cell carcinoma	UTER: Uterus cancer

Completed by (investigator's initials)	Date Completed (dd-mm-yyyy)
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