UNAIDS/WHO WORKING GROUP ON GLOBAL HIV/AIDS AND STI SURVEILLANCE

FIND & WHO WORKING GROUP ON HIV INCIDENCE ASSAYS MEETING REPORT

20–26 FEBRUARY 2016
BOSTON, MA, USA

FIND
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UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance

Global surveillance of HIV and sexually transmitted infections is a joint effort of the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS). The UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance, initiated in November 1996, is the main coordination and implementation mechanism for UNAIDS and WHO to compile the best information available and to improve the quality of data needed for informed decision-making and planning at the national, regional and global levels.

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ABBREVIATIONS

ART	antiretroviral therapy
ARV	antiretroviral
CDC	United States Centers for Disease Prevention and Control
CEPHIA	Consortium for the Evaluation of the Performance of HIV Incidence Assays
CI	confidence interval
DBS	dried blood spot
DREAMS	Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe women
FIND	Foundation for Innovative New Diagnostics
FRR	false recent rate
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HPTN	HIV Prevention Trials Network
IDE	immunodominant epitope
LAg	limiting antigen
MDRI	mean duration of recent infection
PBS	phosphate-buffered saline
PCR	polymerase chain reaction
PEPFAR	United States President's Emergency Plan for AIDS Relief
PrEP	pre-exposure prophylaxis
RT-PCR	reverse-transcription polymerase chain reaction
SACEMA	South African Centre for Epidemiological Modelling and Analysis
SHIMS	Swaziland HIV Incidence Measurement Survey

1. BACKGROUND

In 2008, WHO established a Technical HIV Incidence Assay Working Group to examine the issues and challenges involved in estimating HIV incidence using assays. This Group comprises epidemiologists, laboratory specialists and public health officials and has worked to standardize the terms in the fields of assay calibration and validation. Several meetings to advance the agenda have been held, and copies of the reports are available on the Working Group web page (www.who.int/diagnostics_laboratory/links/hiv_incidence_assay/en).

These meetings have been successful in bringing together a wide group of assay users, especially from countries affected by the HIV epidemic that may consider using HIV incidence assays in the future, together with experts in applying laboratory-based methods for estimating HIV incidence. The importance of HIV incidence as a key indicator of the success or failure of national HIV programmes has been highlighted, and health ministries clearly need to be aware of the complexities in producing estimates based on data generated by the currently available assays.

In collaboration with the United States Centers for Disease Control and Prevention (CDC), the Working Group produced a guidance document on how to estimate HIV incidence at the population level using HIV incidence assays in cross-sectional studies (*1*). In 2010, the Bill & Melinda Gates Foundation adjudicated a grant proposal to Public Health England and the Blood Systems Research Institute to continue laboratory work on existing HIV incidence assays. The Consortium for the Evaluation of the Performance of HIV Incidence Assays (CEPHIA) was established, which aims to validate existing and future HIV incidence assays, compare results from existing assays with direct incidence measurements and identify the key parameters to enable assay results to be interpreted correctly.

The Working Group last convened in October 2014 in Barcelona, Spain; this was funded by WHO, the CDC, CEPHIA and UNAIDS (*2*). Following this meeting, a technical update was published for the application of HIV incidence assays for surveillance (*3*), which was also incorporated into the new guidelines for monitoring the impact of the HIV epidemic using population-based surveys (*4*).

The purpose of the 2016 meeting of the Working Group was to convene a group of key opinion leaders in the field to discuss critical issues outstanding after the previous Working Group meeting. The main objectives of this meeting were:

- to obtain consensus on the mean duration of recent infection (MDRI) for the CDC-derived limiting antigen (LAg) assays (from Sedia Biosciences Corporation and Maxim Biomedical) and variability among HIV subtypes;
- to present the performance characteristics of five further incidence assays studied as part of the CEPHIA evaluation;
- to present the evaluation of recent infection testing algorithms including testing for viral load and for antiretroviral (ARV) medicines;
- to release the revised version of the sample size calculation tool by the developer, recommended by WHO (*5*);
- to determine methods for qualifying new kit lots made by commercial partners to ensure LAg quality management systems during manufacturing processes;
- to establish a proficiency testing programme for the LAg assay that may be expanded to other assays as the need for external quality assurance is demonstrated; and
- to obtain consensus on target product profiles for tests for recent HIV infection.

The 2016 Working Group meeting in Boston was funded by UNAIDS, the Foundation for Innovative New Diagnostics (FIND) and WHO.

2. METHODS OF WORK

HIV incidence and mortality remain important indicators for the Sustainable Development Goals and are used as target measures, especially by the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and the United States President's Emergency Plan for AIDS Relief (PEPFAR).

The current role of the Working Group is:

- to review and document the calibration, performance and validation of HIV incidence assays;
- to create a catalogue of studies reporting on assay validation and calibration;
- to define the assay development pathway and target product profiles; and
- to obtain consensus on statistical issues and terms.

Since publication, the guidance on how to apply incidence assays has since been accompanied by two technical updates (*3*).

The critical path to improve HIV incidence testing incorporates market, technical and regulatory issues and requires developing normative guidance, advocacy and support. Market issues include the need for a reliable commercial supplier of incidence assays; technical issues include the need for specimens to standardize the calibration and validation of assays; regulatory issues include identifying and executing a clear regulatory path to independent validation and approved use in the market. WHO/UNAIDS will need to develop updated guidance to be adopted by the HIV community, with dedicated individuals supporting new users.

Understanding of the characteristics and limitations of HIV incidence assays has improved, including the need for large sample sizes in low-incidence areas. However, more work is needed to be able to expand their use to produce subnational estimates and estimates for key populations. Challenges include the scaling up of antiretroviral therapy (ART) and whether this will require ARV testing in addition to viral load in a recent infection testing algorithm. The effect of early or discontinued ART or a history of pre-exposure prophylaxis (PrEP) use is still being evaluated, but recent studies demonstrate that these can affect recency assays, such as slowing antibody avidity maturation. In addition, a local estimate of the false recent ratio (FRR) is required, which will become increasingly difficult with widespread ART use. The FRR varies by HIV subtype, being especially high among people with subtype D and is unknown for subtypes CRF02_AG and CRF01_AE. Following these outstanding issues, and specifically in the context of the new "treat all" guidelines, recommendations on best practices in the context of tests for recent infection are needed.