RECENT HIV INFECTION TESTS: MOVING PAST PROOF OF CONCEPT

FIND
Because diagnosis matters

The need for better tests to estimate HIV incidence

Ending the HIV epidemic by 2030 will require a major increase in efforts and resources. According to UNAIDS, simply maintaining the AIDS response at 2013 levels will result in a rebound of the epidemic, whereas an increase of US$ 8-12 billion per year from the current levels of approximately US$ 20 billion will be needed to end the epidemic by 2030.[1]

As we call on international donors and national governments to increase their funding commitments, the pressure is growing to better measure the effectiveness of these investments.

Using a data-driven approach to designing and evaluating interventions is key to assessing the efficacy and efficiency of HIV investments. Until recently, this proved to be a major challenge due to the fundamental difficulty of accurately estimating HIV incidence[2] – i.e. measuring the rate of new infections. Now, new approaches to estimating HIV incidence are available.

These novel methods revolve around the use of laboratory-based tests that can determine whether an HIV infection was contracted within the previous year. The combination of the Limiting Antigen (LAg)-Avidity Enzyme Immunoassay with viral load, while useful for single incidence estimates in the highest incidence settings, does not address all current needs for incidence measurement. It requires large survey sample sizes to obtain reliable estimates, which limits utility to countries with high incidence and prevalence rates. In addition, these tests cannot reliably detect reductions in incidence over time. According to statistical models developed by SACEMA (South African Centre for Epidemiological Modelling and Analysis), results generated using current tools will not be precise enough to enable comparisons with similar surveys done at a later time.

What a new, better performing test can offer:

Improved performance will enable cost-effective and accurate measurement of HIV incidence by reducing required survey sample sizes. This would allow countries and the global community to:

- Accurately determine baselines and monitor the trajectory of local, national or regional HIV epidemics—before and after specific interventions.
- Ensure that investments in HIV prevention strategies are targeting the correct populations at the correct time, and aid in the design of clinical trials for emerging drugs, treatment regimens and prevention interventions, by identifying and focusing on populations with the highest incidence.
- Assess the impact of HIV prevention programmes by using incidence as a key metric.

The use of improved laboratory-based biological assays in national HIV surveys can provide more accurate, representative and timely HIV incidence estimates in a wide variety of contexts.

Despite these limitations, the demand for HIV incidence testing is growing. The WHO released new guidelines in 2015 stating that incidence should be used as a key indicator for evaluating the impact of HIV prevention programmes in high prevalence (>5%) and high incidence rate (>0.3%) settings.[4] Now, numerous countries in sub-Saharan Africa are planning to employ recent infection testing algorithms, funded by PEPFAR, as part of their national HIV surveys going forward.

It is clear that a second-generation HIV incidence test needs to be developed in order to meet growing demand in a more efficient and cost-effective manner. Research and development must be accelerated for technologies that would expand the utility of these tests by reducing required sample sizes, eliminating the need for supplemental tests and improving the accuracy of the incidence estimates obtained from these measurements.

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Research and development of recent infection tests: challenges and opportunities

Research on HIV incidence tests has been ongoing for several years. In 2012, this work received an important boost when the National Institute of Allergy and Infectious Disease and the Bill & Melinda Gates Foundation awarded new biomarker discovery and development grants that will expire in early 2016. Out of these grants, at least two promising sets of biomarkers have emerged with the potential to result in a new, game-changing test.

If these biomarkers are successfully validated in the proof of concept stage, an intense effort will be required to move through the process of development, qualification, evaluation and commercialization to bring an improved test to market. There is a wide variety of stakeholders involved in bringing new tests to market. Coordinating between them to ensure that final products meet country needs is critical. Resources that are essential to test development, such as specimen banks, must be supported and enhanced.

The challenge is not only in the work that lies ahead, but in how the next steps will be financed. In the landscape of test development, there is a profound funding gap between the discovery phase and the implementation of new tests. In particular, market-based incentives for surveillance-based tests are limited for private companies. As such, public donor support will be critical in moving this work forward.

FIND's capacity to translate technical advances into tools and policies that support HIV prevention

Realizing the potential for improved tests

New biomarkers associated with recent HIV-1 infection have been identified through a variety of screening approaches including:

- Hypothesis-driven testing for specific anti-HIV antibodies known to fluctuate post-infection in patient plasma, including binding avidity;
- Screening of a random peptoid shape library for antibodies whose concentrations change with time since infection; and
- Measurement of markers of inflammatory bowel disease, including cytokines.

With the support of CEPHIA (the Consortium for the Evaluation & Performance of HIV Incidence Assays), which provides specimens from a curated biorepository and analysis support, some of these novel biomarkers are poised to move into the assay development stage. Advancement through this next stage will require investment in the range of US$ 2-5 million to support the transition from a research grade test to a robust, packageable and quality-assured product.

FIND is working with potential assay developers and academic research groups to establish a partnership with these goals in mind. It is estimated that it may take two to three years before the new assay is widely available.

FIND is the only non-profit organization whose sole focus is to increase access to diagnostics for diseases of poverty. Through this work, FIND enables accurate treatment, targeted healthcare interventions and measurement of progress for disease elimination and eradication.

FIND catalyses the development of needed diagnostic tools, guides their use, informs policy and works to accelerate access to new and existing diagnostic solutions. FIND's strengths lie in its ability to remain a neutral player working to fill gaps while providing coordination between assay developers, users and implementers (including health ministries), funders and normative agencies.

FIND has extensive experience in providing country-level diagnostics implementation support and is well-versed in assisting countries in the development of national plans for implementation of new diagnostics, supporting early implementation of new technologies, designing and instituting external quality assurance programmes, and building and strengthening laboratory capacity, as well as quality management and accreditation systems. FIND has a roster of experienced staff and consultants based in several countries, including but not limited to Kenya, Uganda and South Africa, with expertise in laboratory strengthening and training capacity.

In the area of HIV incidence assays, FIND has been working closely with WHO, UNAIDS, CDC, CEPHIA (the Consortium for the Evaluation & Performance of HIV Incidence Assays) and its individual member organizations. As a result, FIND is able to draw on its own expertise and that of others, as needed. This flexibility allows FIND to fill a critical role in the implementation of recent infection tests to optimize HIV incidence estimation, including in:

- Survey planning, such as support for survey size calculations;
- Training for lab staff and/or train-the-trainer models;
- Supporting biomarker and assay evaluation work;
- Supporting data analysis and interpretation.

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2. IACPWG. More & better information to tackle HIV epidemics: towards improved HIV incidence assays. *PLoS Med* **8**, e1001045, doi:10.1371/journal.pmed.1001045 (2011).
3. Kassanjee, R. *et al.* Independent assessment of candidate HIV incidence assays on specimens in the CEPHIA repository. *AIDS* **28**, 2439-2449, doi:10.1097/QAD.0000000000000429 (2014).
4. Joint United Nations Programme on HIV/AIDS (UNAIDS), Monitoring HIV Impact Using Population Based Surveys, UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance, 2015.