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Study of laboratory tests to discern ‘recently’ from ‘non-recently’ acquired HIV infection opens new possibilities for HIV surveillance and clinical management of HIV

In collaboration with a multi-national team of researchers, the Stellenbosch University based South African Centre for Epidemiological Modelling and Analysis (a.k.a. SACEMA, a Department of Science and Technology/National Research Foundation ‘Centre of Excellence’ www.sacema.org) has published a benchmark-setting evaluation of HIV disease-staging diagnostic tests which have the potential to revolutionise HIV incidence surveillance (ref 1. A short video abstract is available - ref 2). It is a persistent challenge that disease incidence (the rate of occurrence of new cases) is much harder to measure than disease prevalence (the fraction of a population which has the condition at a point in time). Incidence is much more informative, as it tells us about recent disease transmission, and hence about effectiveness of efforts to curb transmission.

Incidence estimation is more than an academic technical challenge. Charged debate ensues when politicians, activists, and researchers struggle to agree on what the epidemiological trends actually are. Prevalence of HIV is widely tracked and cited, but very difficult to interpret, as it emerges over a long time scale of interplay between new infections and post infection survival. For example (such as has occurred in South Africa) in the context of a rapidly growing effective antiretroviral treatment programme, an established high stable prevalence is expected to be nudged upwards as mortality decreases, even if incidence actually declines. Alternatively, a decline from high prevalence peaks, in the absence of treatment (as has been seen in numerous countries) could initially be a sign of alarming mortality increases, rather than decreased incidence.

The work just published in the high profile journal AIDS, is the first landmark publication from a major initiative, funded by the Bill & Melinda Gates Foundation, known as the Consortium for the Evaluation and Performance of HIV Incidence Assays (CEPHIA <http://www.incidence-estimation.org/page/cephia>).

Reshma Kassanjee of SACEMA, lead statistician and first author of the article, explains:

Surveys which test not merely for HIV infection, but for carefully defined ‘recent infection’, make it possible to understand not just who is infected at a point in time, but also at what rate new infections have been occurring in the recent past. The measurement of incidence is of great epidemiological importance, especially as funders and programme implementers try to allocate limited resources and evaluate interventions. Until now, it has not been possible to provide a consistent overview of the relative merits of the numerous proposed ‘recent infection tests’, which for some years have attracted considerable, but uncoordinated, attention. Our investigation reveals that, while there are numerous tests which qualitatively appear to do a good job of distinguishing between ‘recent’ and ‘non-recent’ infection, none as yet, used alone, defines a notion of ‘recent infection’ that is sufficiently robust for widespread use in the surveillance applications which are currently attracting interest – namely population-level incidence estimation at the regional, national or district scale.

Alex Welte, SACEMA director and a co-author on the study, adds:

SACEMA has worked extensively in coordination with the UN bodies and key collaborators, such as UK and US academics and government agencies, to develop a whole new approach to this concept of testing for ‘recent infection’ for surveillance purposes (see ref 4,5,8) . This is our most significant application to date of the theory and tools we have been working on for 7 years.

The CEPHIA consortium has been active for three years. Our US collaborators (at University of California – San Francisco, and Blood Systems Research Institute – also in San Francisco) have assembled and characterised a unique repository of specimens. Lab work done on these specimens enables us to give concrete quantitative meaning to ‘recent infection’ as defined by laboratory

biomarkers. Our UK partners (in the Virology reference laboratory at Public Health England) have led the standardisation of laboratory procedures; a critical step in moving these tests from research platforms towards tradable technology.

This first high profile research output of the consortium (we have presented preliminary results at conferences) provides a foundation for considerable additional analyses of the data now rapidly converging on our database from participating laboratories. Recent infection tests have been used in the field for some years, but there is considerable controversy about the correct analysis and interpretation. CEPHIA is having deep impact by sharing data and tools, and building consensus.

At the end of the year, the CEPHIA consortium will complete its first major phase, which includes benchmarking further *recent infection* assays and exploring combinations of separately developed biomarkers into more complex tests, or 'algorithms'. CEPHIA phase II includes the expansion of the specimen repository through ongoing studies, and supporting, through the provision of specimens and analytical tools, numerous independent 'biomarker discovery' projects.

SACEMA is also involved in a World health Organisation (WHO) working group which has helped coordinate guidelines for the use of recent infection tests for surveillance, and is hosting and facilitating a WHO sponsored training workshop on this work in Stellenbosch in September. A SACEMA policy brief (ref 3) has been released, on the occasion of the appearance of the article in AIDS, to provide a qualitative briefing note on recent infection testing technology and its applicability.

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1. Kassinjee R, Pilcher CD, Keating SM, et al.; Consortium for the Evaluation and Performance of HIV Incidence Assays (CEPHIA). Independent assessment of candidate HIV incidence assays on specimens in the CEPHIA repository. AIDS. 2014 Oct 23;28(16):2439-49.[View article by clicking here](#)
2. <http://links.lww.com/QAD/A569>
3. http://sacema.org/uploads/announcements/2014_aids_policy_brief/PolicyBrief_CEPHIA_AIDS.pdf
4. See also CEPHIA collaboration website <http://www.incidence-estimation.org/page/cephia>