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Cost-Effectiveness of Nucleic Acid Amplification Tests for Identifying Acute HIV Infections

We read with interest the study by Gous et al. (2) evaluating the utility of HIV nucleic acid amplification tests (NAAT) of pooled HIV seronegative serum samples to identify acute HIV infections (AHI).

Four of 3,005 seronegative sera were identified as RNA positive by 211 NAAT at a cost of $7.16 per sample over and above the cost of HIV serology alone.

The multitude of benefits from early diagnosis of HIV infection are undisputed; however, the most meaningful value to determine feasibility is the cost per additional case identified that would have been missed by antibody testing alone. In this study, this cost was $5,392.

Furthermore, careful consideration needs to be given to the possibility of false-positive NAAT results. Various RNA assays cause occasional false-positive results, mostly reporting low viral load values (6, 7, 8) but rarely even >10,000 copies/ml (1). The paper does not discuss this possibility. One of the four positive samples had a very low viral load of 84 copies/ml; given the small input volume of only 100 μl, this is unlikely to cause a positive pool. Two others had viral loads of 3,430 and 11,900 copies/ml. Such low levels are unexpected in AHI and may suggest false positives.

If only two instead of four samples were truly positive, the prevalence rate would be halved and the cost per additional case identified would double to $10,784.

Finally, it is unclear why a fourth-generation enzyme-linked immunosorbent assay (ELISA) (combined antigen/antibody detection) is negative in the presence of a viral load as high as 1.87×10^6 copies/ml. HIV viral load and p24 levels in the peripheral blood correlate well (9), and the Abbott AxSym fourth-generation HIV assay used by Gous et al. is very sensitive (4). During two evaluations, this assay never reported a negative result at viral loads in excess of 8×10^4 copies/ml (5, 10). However, a second diagnostic window may occasionally cause false-negative results in combined antigen/antibody tests.

Another study of pooled NAAT following third-generation ELISA testing established that this strategy will be cost-effective only in settings with a very high HIV incidence (3). Using fourth-generation ELISAs, better at detecting acute HIV infections, may further reduce cost-effectiveness. The same study highlighted the need for timely delivery of NAAT results, as a public health benefit results from decreasing the potential for transmission due to high infectivity during AHI. It was calculated that the cost-effectiveness of pooled NAAT screening may be improved when notifications of all positive results are made within 7 days, although it may still be beyond generally accepted threshold values.

The title of the study by Gous et al. asks a difficult question, especially under circumstances where resource constraints not only impact the technical aspects of testing but also the logistics. The answer should not only take the cost of laboratory testing, reporting, and clinical management into account but also the ability of the astute physician to retain a high index of suspicion and consequently repeat serological tests, which may eliminate or at least decrease the necessity for NAAT.

REFERENCES

1. **de Mendoza, C., A. Holguín, and V. Soriano.** 1998. False positives for HIV using commercial viral load quantification assays. AIDS **12:**2076–2077.
2. **Gous, N., L. Scott, O. Perovic, F. Venter, and W. Stevens.** 2010. Should South Africa be performing nucleic acid testing on HIV enzyme-linked immunosorbent assay-negative samples? J. Clin. Microbiol. **48:**3407–3409.
3. **Hutchinson, A. B., et al.** 2010. Cost-effectiveness of pooled nucleic acid amplification testing for acute HIV infection after third-generation HIV antibody screening and rapid testing in the United States: a comparison of three public health settings. PLoS Med. **7:**e1000342.
4. **Ly, T. D., et al.** 2004. Evaluation of the sensitivity and specificity of six HIV combined p24 antigen and antibody assays. J. Virol. Methods **122:**185–194.
5. **Malm, K., M. von Sydow, and S. Andersson.** 2009. Performance of three automated fourth-generation combined HIV antigen/antibody assays in large-scale screening of blood donors and clinical samples. Transfus. Med. **19:**78–88.
6. **Nesheim, S., et al.** 2003. Quantitative RNA testing for diagnosis of HIV-infected infants. J. Acquir. Immune Defic. Syndr. **32:**192–195.
7. **Rich, J. D., et al.** 1999. Misdiagnosis of HIV infection by HIV-1 plasma viral load testing: a case series. Ann. Intern. Med. **130:**37–39.
8. **Rouet, F., et al.** 2001. Early diagnosis of paediatric HIV-1 infection among African breast-fed children using a quantitative plasma HIV RNA assay. AIDS **15:**1849–1856.
9. **Schüpbach, J., et al.** 2001. Antiretroviral treatment monitoring with an improved HIV-1 p24 antigen test: an inexpensive alternative to tests for viral RNA. J. Med. Virol. **65:**225–232.
10. **Sickinger, E., et al.** 2004. Multicenter evaluation of a new, automated enzyme-linked immunoassay for detection of human immunodeficiency virus-specific antibodies and antigen. J. Clin. Microbiol. **42:**21–29.

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