Rapid testing strategies for HIV-1 serodiagnosis in high-prevalence African settings

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three different testing algorithms for human immunodeficiency virus (HIV) serodiagnosis were studied. A single, highly sensitive rapid antibody test (Abbott Determine) was compared against:

(i) serial algorithm, where positive results on the first test (Abbott Determine) were confirmed with a more specific second test (Trinity Capillus); and

(ii) a parallel algorithm, where each specimen was tested with two separate rapid tests (Abbott Determine and Trinity Capillus), and discordant results were resolved with a different rapid test (Trinity Serocard).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The target population was a hypothetical cohort of 10,000 individuals in a sub-Saharan African setting with 25% HIV prevalence. The age and gender of the target population were not defined.

Setting
The practice setting was primary care. The economic study was carried out in sub-Saharan Africa.

Dates to which data relate
The effectiveness data related to studies published between 1997 and 2002. The resource data related to a study published in 2003. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a review of published studies and some assumptions or estimates.

Modelling
A decision-tree model was used to compare the benefits (averted incorrect test results) and costs of three testing strategies for HIV serodiagnosis. More specifically, a single-test algorithm was compared with a serial algorithm and a parallel algorithm. There were two possible pathways for the single and serial strategies (positive and negative), while there were three pathways for the parallel strategy (positive, negative and discrepant). The possible ends of all strategies were "positive" and "negative" result, with the serial strategy having an additional end named "undetermined" result.
Outcomes assessed in the review
The outcomes assessed were the seroprevalence of HIV infection and the accuracy of the rapid tests (sensitivity and specificity).

Study designs and other criteria for inclusion in the review
Studies were included if they compared the performance of the rapid tests on blood samples from African populations with that of a "gold" standard diagnostic algorithm (ELISA with confirmatory Western blot, or ELISA with a second confirmatory ELISA).

Sources searched to identify primary studies
The authors searched MEDLINE for relevant studies.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Studies were included if they provided the number of true-positive, false-positive, true-negative and false-negative results.

Number of primary studies included
The authors included 15 studies in the review.

Methods of combining primary studies
The effectiveness data concerning the accuracy of the rapid tests were combined, but the method used was not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The sensitivity of the Abbott Determine rapid test was 100% (95% confidence interval, CI: 99.79 - 100) and the specificity was 99.16% (95% CI: 98.81 - 99.41).

The sensitivity of the Trinity Capillus rapid test was 99.42% (95% CI: 99.10 - 99.62) and the specificity was 99.46% (95% CI: 99.30 - 99.58).

The sensitivity of the Trinity Serocard rapid test was 99.90% (95% CI: 99.63 - 99.97) and the specificity was 99.07% (95% CI: 98.77 - 99.30).

A seroprevalence of HIV infection of 25% was chosen for the baseline. The specific population to which this referred was not stated. The seroprevalence of HIV infection in a population of hospitalised individuals with symptoms suggestive of acquired immune deficiency syndrome was 50%.

Methods used to derive estimates of effectiveness
To augment data from the literature, the authors made an assumption based on a published study.
Estimates of effectiveness and key assumptions
The seroprevalence of HIV infection in a population of blood donors was assumed to be 5%.

Measure of benefits used in the economic analysis
The health benefits used in the study were incorrect result averted, indeterminate result averted, false-positive result averted and false-negative result averted.

Direct costs
The direct costs of the health service were included in the analysis. Only the immediate costs related to diagnostic testing were included. The direct costs reported consisted of the costs of the HIV rapid test kits and the costs of labour per test performed. The quantities and the costs were reported separately. The unit costs of the HIV rapid tests were derived from a published study carried out in Lusaka, Zambia. The daily wage of a laboratory technician in Lusaka, and the number of daily HIV tests performed, were based on authors' assumptions. The costs were not discounted because they were incurred during a short time. The price year was not reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
No indirect costs were included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed. These evaluated the robustness of the results to the accuracy estimates of the rapid tests, using the lower limit of the 95% CIs. Two additional HIV prevalence scenarios were also evaluated (HIV prevalence in the population of 50% and 5%).

Estimated benefits used in the economic analysis
The single-test algorithm resulted in 63 false positives and no false negatives or indeterminate results. The serial algorithm resulted in 77 indeterminate results, but no false positives or negatives. The parallel algorithm provided one false positive, but no indeterminate results or false negatives.

Cost results
The total cost of the single-test algorithm was $10,500, while that of the serial algorithm was $18,060 and that of the parallel algorithms $40,299.

Synthesis of costs and benefits
The costs and benefits were combined by calculating an incremental cost-effectiveness ratio (ICER).

The ICER of the serial strategy against the single test was $120 per additional incorrect result averted in a population with 25% HIV prevalence.

The ICER of the parallel strategy against the single test was $480 per additional incorrect result averted in a population with 25% HIV prevalence.
The ICER of the parallel strategy against the serial strategy was $288 per additional indeterminate result averted in a population with 25% HIV prevalence.

The sensitivity analysis showed that the results were sensitive to the accuracy of the rapid tests. In a population with 25% HIV prevalence and using the lowest estimates of test accuracy, the ICER of the serial algorithm versus the single-test test algorithm was $87 per incorrect result avoided and that for the parallel algorithm versus the serial algorithm was $324 per incorrect result avoided. Also, when the parallel strategy was used instead of the serial strategy, the cost per each additional incorrect result averted was $5,551 and the cost per each indeterminate result averted was $200.

The results were also sensitive to the value of HIV prevalence in the population. With a 50% prevalence of HIV in the population and the lowest estimates of test accuracy, the ICER of the serial strategy versus the single-test strategy increased to $252 per incorrect result averted, while the cost per indeterminate result averted from using the parallel strategy compared with the serial strategy decreased to $143.

With a 5% prevalence of HIV in the population, the serial strategy became extendedly dominated by the parallel algorithm in terms of incorrect results avoided. This means that, although the serial strategy was cheaper than the parallel strategy, its ICER compared with a single test was higher, much higher in this case. The ICER of the parallel strategy compared with the single-test strategy decreased to $269 per incorrect result avoided.

Authors' conclusions
In any setting, both the serial and parallel algorithms resulted in fewer incorrect results than the single test, but they were more costly. Although the parallel strategy yielded fewer incorrect results than the serial strategy, it was more costly.

CRD COMMENTARY - Selection of comparators
The justification provided for the different comparators used was that combination algorithms might perform better than individual tests. You should decide if these are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state whether a systematic review of the literature was undertaken, although simple inclusion criteria were reported. The authors justified their assumptions with reference to the medical literature. The estimates of effectiveness were combined, but the method used was not reported. However, sensitivity analyses were conducted, which enhances the transferability of the results.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using a decision analytic model, which was appropriate. The measures of benefit (incorrect results avoided, indeterminate results avoided, and false positives or negatives avoided) were valid, but present a limitation in terms of the comparability of the interventions in relation to other health care programmes. The authors acknowledged this limitation and stated that a formal cost-effectiveness analysis would have considered the consequences of the incorrect results.

Validity of estimate of costs
The study perspective was not stated, but the direct costs included public health service costs. Some relevant costs were omitted from the analysis. More specifically, the costs of implementing a national screening programme, the costs of training staff, and the costs resulting from incorrect testing results. Consequently, the costs of the interventions might have been underestimated. However, the authors acknowledged this limitation and justified the omission of test-related costs. The unit costs were presented separately, which will enhance the generalisability to other settings, but it is unclear whether the prices in Lusaka, Zambia, are representative of the rest of sub-Saharan Africa. The resource use quantities used in the study were derived from authors' assumptions. No sensitivity analyses were performed on either the resource use quantities or on the unit costs used, and this may limit the interpretation of the study findings.
Other issues
The authors did not compare their findings with those from other studies. They did, however, address the issue of generalisability to other settings. The authors do not appear to have presented their results selectively. They acknowledged a limitation to their study in that the non-immediate costs associated with the screening strategies were not included.

Implications of the study
The authors suggested that a parallel algorithm might be too expensive for many developing world settings, despite avoiding indeterminate results. They recommended the serial algorithm as appropriate for the following clinical settings: voluntary counselling and testing, prevention of mother-to-child treatment, transfusion safety, and for testing sick patients with suspected HIV infection. The authors recommended the single test for the surveillance of populations.

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