A clinical utility-risk-benefit analysis for HIV self-testing

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BACKGROUND
As countries work to achieve the United Nation’s “90-90-90” testing and treatment targets, many countries are adopting WHO’s recommendation for HIV self-testing as an additional HIV testing approach. Many self-tests can use an HIV rapid diagnostic test (HIV RDT) to correctly achieve results similar to those from testing laboratories. As HIV RDT does not provide an HIV status diagnosis, concerns about potential false reactive and false non-reactive results remain. Thus, we conducted a clinical utility-risk-benefit analysis to establish minimum performance thresholds for HIV RDTs which provide health benefits to be achieved.

METHODS
To assess HIV RDT clinical utility and weight performance-related risks and benefits, sensitivity (0.5-0.95), specificity (0.5-1.0), HIV prevalence (0.1-1.0), linkage to care (0-100%) and treatment to prevention (0-100%) were considered. For each scenario, the base case, and the low and high uncertainty were derived from distributions to generate a range of sensitivity and linkage to care to determine the benefit threshold. The benefit threshold was derived from a threshold utility function by multiplying the number of true reactive results by the true non-reactive results. The benefit threshold is the number of false positive results (also known as any false results) that are acceptable. The proportion of scenarios with positive test benefit was calculated.

RESULTS
61% of scenarios with 90% sensitivity and 99% specificity had positive benefit on the lives of high prevalence and high linkage to care. As HIV prevalence decreased to 0.1%, positive test benefit decreased to 0.95% specificity and 75% sensitivity. For very low prevalence scenarios (prevalence < 0.1%), not benefit greatly increased as sensitivity increased from 95% to 99%. Linkage to prevention drove net benefit; whereas moderate (50-100%) benefit was achieved at 100% specificity, whereas very low (30-50%) sensitivity was needed. Linkage to care varied from 50% to 100%, with modest impact except in very high prevalence settings, e.g., among female sex workers in Johannesburg. Net positive benefit for high prevalence was not observed at HIV RDT to care to be zero.

Table 1a. Percent of situations with net positive results, overall

Table 1b. Percent of situations with net positive results, overall (100%–99%)

Table 1c. Per cent of situations with net positive results, overall (99%–90%)

Table 1d. Percent of situations with net positive results, overall (90%–80%)

Table 1e. Percent of situations with net positive results, overall (80%–70%)

Table 1f. Percent of situations with net positive results, overall (70%–60%)

Table 1g. Percent of situations with net positive results, overall (60%–50%)

Table 1h. Percent of situations with net positive results, overall (50%–40%)

Table 1i. Percent of situations with net positive results, overall (40%–30%)

Table 1j. Percent of situations with net positive results, overall (30%–20%)

Table 1k. Percent of situations with net positive results, overall (20%–10%)

Table 1l. Percent of situations with net positive results, overall (10%–0%)

Table 1m. Percent of situations with net positive results, overall (0%–0%)

Figure 1. Subset of scenarios with net positive results (base case scenario: linkage to care 100%)

Figure 2. Varying weights of risk and benefit by HIV prevalence

Figure 3. Case Example female sex workers in Johannesburg, South Africa

TABLE\n
Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity.

Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity (100%–99%)

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Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity (50%–40%)

Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity (40%–30%)

Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity (30%–20%)

Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity (20%–10%)

Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity (10%–0%)

Table: Comparison of scenarios with net positive results with various combinations of sensitivity and specificity (0%–0%)

CONCLUSION
In the majority of scenarios, risks were exceeded by the benefits of diagnosis and linkage to HIV prevention and treatment services.

LIMITATIONS
This clinical utility analysis assessed HIV RDT risk and benefit based on performance alone and did not consider additional factors such as cost or feasibility.

In addition, the weights used in the models were derived from expert opinion due to the absence of sufficient data. We are currently exploring updating this analysis using data from the HIV self-test Africa (HSTAF) project.

This analysis has important implications for countries considering the introduction of HIV RDTs, as it provides a framework for evaluating the potential benefits and risks of HIV RDTs in different settings.