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

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BACKGROUND
As countries work to achieve the United Nations’ “90-90-90” testing and treatment targets, many countries are adopting HIV self-testing (HIVST) as an additional HIV testing approach. Many self-testers can use an HIV rapid diagnostic test (RDT) correctly and achieve results similar to trained testers. Although HIVST does not provide an HIV-positive diagnosis, some concern about potential false reactive and false non-reactive self-test results remains. Thus, we conducted a clinical utility benefit-risk analysis to establish a minimum performance threshold for HIVST at which public health benefit can be achieved.

METHODS
To assess HIVST's clinical utility and weigh performance-related risks and benefits, sensitivity (65-99.8%), specificity (90-100%) and linkage to prevention (10-50%) were considered. Scenarios were based on literature review and available programme data from South Africa. Different cases were characterized by varying levels of these factors were simulated. We then sampled from distributions to generate each scenario and non-simulations excluding scenarios in which no benefit was achieved. A net benefit score was derived as Total Benefit (calculated as the sum of true reactive linked to care multiplied by three and the true non-reactive multiplied by two). The weight for false non-reactives, false reactivities, true reactive linked to care and true non-reactive linked to prevention were weighted based on expert consultation. The proportion of scenarios with positive net benefit was calculated.

RESULTS
61% of scenarios with ≥70% sensitivity and ≥90% specificity yielded greater benefit than risk. In high prevalence scenarios (prevalence ≥5-10%), net benefit marginally increased when sensitivity increased from 70% to 90%. Linkage to care (≥80% specificity) and ≥70% sensitivity. For very high prevalence levels (prevalence ≥50-100%), ≥90% specificity and ≥70% sensitivity. In high prevalence scenarios (prevalence ≥5-10%), net benefit marginally increased when sensitivity increased from 70% to 90%. Linkage to care (≥80% specificity) and ≥70% sensitivity. For very high prevalence levels (prevalence ≥50-100%), ≥90% specificity and ≥70% sensitivity. In high prevalence scenarios (prevalence ≥5-10%), net benefit marginally increased when sensitivity increased from 70% to 90%. Linkage to care (≥80% specificity) and ≥70% sensitivity. For very high prevalence levels (prevalence ≥50-100%), ≥90% specificity and ≥70% sensitivity. 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CONCLUSION
In the majority of scenarios, risks were exceeded by the benefits of diagnosis and linkage to HIV prevention and treatment services. While HIVST’s clinical utility is greatest when performance is greatest, this analysis suggests that net benefit can be achieved even when performance falls below previously acceptable standards (90% specificity and 70% sensitivity) in most settings considered. Provided services linking self-takers to HIV prevention and treatment services are functional. For very high prevalence settings, such as among female sex workers in Johannesburg in South Africa (72%), with very low linkage (21%), ≥80% sensitivity and specificity would be needed to observe a net positive benefit. This emphasizes the need to focus on effective linkage following HIV self-testing, as well as other testing services. The likelihood of achieving a high level of clinical utility using HIVST should be high as studies have shown HIVST kits can achieve sensitivity (80–100%) and specificity (95–100%)

LIMITATIONS
This clinical utility analysis assessed HIVST risk and benefit based on performance alone and did not consider additional social benefits or possible harm.

In addition, the weighting utilized in the model were derived from expert opinion due to the absence of sufficient data. We are currently exploring this analysis using data from the HIV self-test Africa (STAR) project to more explicitly model the consequences of false reactive and non-reactive, as well as the benefits of correct results.