Rapid HIV tests: from meta-analysis to field application

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In *The Lancet Infectious Diseases*, Nitika Pant Pai and colleagues[1] concluded, in a systematic review and meta-analysis, that a rapid point-of-care HIV test, Oraquick, had a slightly lower sensitivity for oral specimens (98·03%) than blood specimens (99·68%), but specificities were similar (99·74% *vs* 99·91%). Although the positive predictive values (PPVs) were similar (98·65% *vs* 98·50%) in high-prevalence settings (HIV prevalence >1%), they identified a lower PPV for oral specimens (88·55%) than blood specimens (97·65%) in lower-prevalence settings.

Meta-analysis has been increasingly used to assess diagnostic methods.[2,3] Although comprehensive guidelines have been issued on the technical aspects of analysis and presentation,[4,5] little has been done to guide practising clinicians in the interpretation of results and the application of these findings. By contrast with the unified concept of effect size in the assessment of therapeutic interventions, the three inter-related sets of diagnostic indices are often a source of confusion to uninformed clinicians. Sensitivity, specificity, and likelihood ratios, being intrinsic test attributes, can be estimated with meta-analysis across different studies. However, most clinicians might prefer the predictive values, which, although highly dependent on prevalence, inform clinical decisions by providing the actual probability that the patient being tested has the target disorder.

Figure: **An HIV testing promotion**

To circumvent the constraint on methods posed by the high dependence of predictive values on target prevalence, Pant Pai and colleagues stratified the included studies into two broad prevalence groups (≤1% and >1%).[1] Initially one might be tempted to attribute the lower PPV of Oraquick for oral specimens in low-prevalence settings to its slightly lower sensitivity. However, from the mathematical relation between the diagnostic indices, specificity, rather than sensitivity, is the key determinant of false-positive rates.[6] Although Oraquick might seem highly specific for both oral and blood specimens (99·74% and 99·91%, respectively), the subtle difference between the false-positive rates among truly negative specimens of 0·26% (100% minus 99.74%) and 0·09% (100% minus 99.91%) proves substantial when the prevalence of the target disorder is less than 1%.

Likelihood ratios have been advocated for refining clinical diagnosis;[7,8] they can be derived directly from sensitivity and specificity, and the post-test odds of a target disorder can be obtained by multiplying the likelihood ratios with the pre-test odds. However, presenting diagnostic test accuracy with likelihood ratios rather than sensitivity and specificity did not affect some physicians' estimates of illness probability in a randomised controlled trial.[9] Pant Pai and colleagues assert that the positive likelihood ratio of Oraquick was lower for oral specimens (383) than blood specimens (1105) but the negative likelihood ratios were similar (0·019 *vs* 0·003).[1] However, closer examination of these ratios shows a less than three-times difference in the positive likelihood ratios but more than six-times difference in the negative likelihood ratios. Because negative likelihood ratios can be mathematically derived from (1–sensitivity)/specificity, the proportionally higher negative likelihood ratio of Oraquick for oral specimens (and

thus less accurate) would be expected from its marginally lower sensitivity estimate.

In clinical practice, we know now that effective antiretroviral treatment reduces HIV-related morbidity and mortality,[10] and through the reduction of the population viral load, such therapy can potentially contribute also to the prevention of transmission.[11] A crucial link between this scientific evidence and the desirable clinical and public health outcomes is the promotion of access to an accurate point-of-care rapid HIV test (figure).[12] Oral fluid-based Oraquick offers the attraction of being more convenient and non-invasive. However, although its better acceptability might promote access to HIV screening, this seems to be at the cost of a substantial false-positive rate,[1,6] even though the estimated specificity of 99·74% might have dwarfed that of most other diagnostic tests in use. This factor must be considered for test interpretation, especially when the availability of such a rapid test allows penetration of screening programme into lower-risk groups. Being dependent on host immunological responses, substantial biological variations would be expected for Oraquick both for oral and blood specimens in the presence and timing of a positive result. Repeat testing after the window period or use of an alternative test is indicated if clinical suspicion remains high despite an initial negative test. Similarly, confirmatory testing is generally thought necessary for a diagnosis with such major implications, even in view of a relatively low chance of false-positive results.

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The end of postoperative antimicrobial prophylaxis?

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In *The Lancet Infectious Diseases*, Hiroshi Imamura and colleagues[1] report data from a randomised controlled trial of antimicrobial prophylaxis in patients having distal gastrectomy for cancer. Patients were randomly assigned to receive 1 g of cefazolin before the incision only or an additional dose once after closure and twice daily for 2 days after surgery. The rates of surgical-site infection were much the same between groups: 9% in the extended treatment group and 5% in the intraoperative alone group. The investigators conclude that postoperative antimicrobial prophylaxis is not recommended for patients undergoing surgery to treat gastric cancer.

This study adds to the data showing the lack of efficacy for postoperative prophylactic antibiotics after closure of the surgical incision, at least in patients with an intact immune system.[2,3] A large meta-analysis[2] including patients having various surgical procedures showed no difference in rates of surgical-site infections between single and multiple doses of prophylactic antibiotics. A Japanese randomised controlled trial[3] of single-dose versus multiple-dose antimicrobial prophylaxis in 501 patients undergoing gastric cancer surgery also showed no benefit to multiple doses. Furthermore, prolonged prophylactic administration leads to increased risks of *Clostridium difficile* disease and antimicrobial resistance.[4]