Summary Table

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<table>
<thead>
<tr>
<th>RDT product</th>
<th>ParaSight-F, Becton Dickinson Diagnostic Systems, Cockeysville, Md.</th>
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<td>Target antigens</td>
<td>HRP2</td>
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<tr>
<td>Comparative standard(s)</td>
<td>Microscopy</td>
</tr>
<tr>
<td>Trial type: Accuracy / Cost-benefits / public health impact / ease of use / behavioural</td>
<td>Accuracy (sensitivity and specificity)/not discussed/moderate/ not discussed/not discussed</td>
</tr>
</tbody>
</table>

*Usefulness of paper (rated by reviewers): 4

**Major findings/implications**

- ParaSight-F has high sensitivity for *P. falciparum* with parasite densities >100-500 parasites/µl with a high level of accuracy for *P. falciparum* diagnosis
- Faint Line intensity can be misread by operators and is confusing
- Strict microscopic reference procedures give greater confidence to comparative interpretation

**Origin:** Peru and Thailand

**Trial type:**

A prospective field study to precisely define ParaSight-F sensitivity and specificity in symptomatic patients and to assess changes in sensitivity at stratified parasitaemia levels.

All patients attending local malaria clinics in Iquitos, Peru and Maesod, Thailand during the study periods and having any of the acceptable symptoms (fever >38°C, headache, HO fever past 72hrs) >15yrs in Thailand and >1yr in Iquitos and were not taking anti malaria treatment currently or during previous two weeks were accepted onto the trial.

Blood samples were collected from all patients into EDTA and precise volumes pipetted onto slides to prepare 3 thick (6µl) and thin (4µl) blood films. One slide was used by local staff for clinical diagnosis and 2 slides were used for the study. The remaining blood was transported to the study laboratory in cool boxes. A ParaSight-F test was performed on all the samples at the test centre for the detection of *Pf* HRP-2 antigen. All ParaSight F tests results were graded from 0.25 to 4 in 6 steps dependent on test line intensity.

Details of the kit were well described and assays were conducted according to manufacturer’s instructions and controls were provided by the manufacturer (recombinant HRP-2) and a negative control was also used. Each investigator and technician was prospectively trained and certified before performing the tests and was reviewed again each week. Technicians were blinded to other results prior to performing the tests. Results graded as un-interpretable were recorded as ‘false’ results for analysis.

**Reference microscopy:**

Two expert certified microscopists independently examined Giemsa stained thick and thin films from slide 1 and 2 for each patient, blinded to each other and ParaSight-F results. Parasitaemia was estimated from asexual parasites seen in 200 fields of the thick film. Sexual gametocytes only were considered negative. Concordance between microscopists was determined and the mean parasitaemia accepted as the true value. Any discordant results were referred to a third observer for confirmed results.

QC of white cell counting systems were put in place and reviewed regularly for both centres.
Data analysis

Device performance end points for sensitivity and specificity were based on the diagnostic results of blood smear interpretation. Device sensitivity was calculated for each of predetermined parasitaemia ranges >0-500, 501-1000, 1001-5000, >5000 parasites/µl. Confidence intervals were computed for device sensitivity and specificity assumed that the diagnostic accuracy of the test followed a binomial distribution.

Results and analysis:

3,006 eligible self presenting symptomatic patients were enrolled into the study, 844 (28%) from Peru and 2162 from Thailand. 13 subsequently were removed and 2993 had blood samples taken.

5 were unsuitable for technical reasons and results from 2, 988 were available for analysis.

1283 cases of malaria were detected microscopically, with 547 *P falciparum*, 658 *P vivax* and 2 *P malariae* and 31 with mixed infection of *Pf/Pv*. 1750 were found negative by microscopy.

183 discordant results between the two microscopists requiring resolution by third microscopist, this was usually on parasitaemia calculations or on presence of parasites. In both cases very low density of parasites were present ParaSight-F gave false negative results in 14/82 patients with 0-500 parasites/µl, other false negatives occurred less frequently with higher parasite densities (12.9% at 501-1000p/µl, 1.9% at 1001-5000p/µl and 2.1% at > 5000p/µl).

The latter result is disconcerting.

ParaSight-F false positive results (microscopy negative) occurred in 14.2% (249 of 1,750 negatives) and in cases of non-falciparum malaria false positives were 14.6%.

32.3% of mixed infections which contained asexual parasites of *P falciparum* gave negative results with ParaSight-F. However as it was not possible to determine the density of parasites in this set, they were removed from the calculation of device performance.

Overall sensitivity for the RDT was 95% (CI 93-99%) for detection of *P falciparum* infection, with Peru arm 89% and Thai arm 97%.

Overall device sensitivity for density >1000 parasites/µl was >90% with progressive decline in lower ranges.

Specificity for ParaSight-F was 86% (Peru 95% and Thailand 82%)

Line intensity:

92.6% of positive results gave a line intensity of >1 by ParaSight-F and 96.9% of negative results by ParaSight-F gave readings of 0.05. 32 (1.8% of samples negative by microscopy generated line intensities of > 1).

Low sensitivity with parasitaemia of >0-100 p/µl was observed but the RDT did detect 90% of *P falciparum* cases in the range of 101-500 p/µl.

Modifying the definition of a negative to include faint lines improved device specificity but not sensitivity.

Implications

The ParaSight-F RDT provided an accurate detection of parasitaemia across two study sites and across multiple levels of parasite densities. Results indicated that for *P falciparum* parasitaemia levels > 100p/µl the device had high sensitivity. Rigorous microscopic reference methods were used in this trial.

*Usefulness of paper (rated by reviewers): 4*

* 1. No direct relevance. 2. Very unlikely to influence current practice. 3. Likely to influence current practice in some settings. 4. Likely to influence current practice in many areas. 5. Highly likely to influence current practice in many areas.

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