Table 1 Description of RDT types included in the review

Type of test	Antibody combinations	Possible results
Type 1	HRP-2 (*P. Falciparum*-specific)	No Pf; Pf; invalid
Type 2	HRP-2 (*P. Falciparum*-specific) and aldolase (pan-specific)	No malaria; Pf or mixed; Pv, Pf and/or Pm; invalid
Type 3	HRP-2 (*P. Falciparum*-specific) and pLDH (pan-specific)	No malaria; Pf or mixed; Pv, Pf and/or Pm; invalid
Type 4	pLDH (*P. Falciparum*-specific) and pLDH (pan-specific)	No malaria; Pf or mixed; Pv, Pf and/or Pm; invalid
Type 5	pLDH (*P. Falciparum*-specific) and pLDH (*P. vivax*-specific)	No malaria; Pf; Pv; Pf and Pv; invalid

Table 2 Average sensitivities and specificities in meta-analyses by type of test and by antibody

RDT type	Number of studies	Sensitivity (95% CI)	Specificity (95% CI)
HRP-2 (Types 1–3)	75	95.0 (93.5–96.2)	95.2 (93.4–99.4)
Type 1	65	94.8 (93.1–96.1)	95.2 (93.2–96.7)
Type 2	8	96.0 (94.0–97.3)	95.3 (87.3–98.3)
Type 3	5	99.5 (71.0–100)	90.6 (80.5–95.7)
pLDH (Types 4 and 5)	19	93.2 (88.0–96.2)	98.5 (96.7–99.4)
Type 4	16	91.5 (84.7–95.3)	98.7 (96.9–99.5)
Type 5	3	98.4 (95.1–99.5)	97.5 (93.5–99.1)

CI: confidence interval.

P. falciparum would be 34 with Type 1 tests, and 9 with Type 4 tests.

The results show that sensitivity and specificity of all RDT types is such that they can be used to extend the access of diagnostic services for uncomplicated *P. falciparum* malaria. Difference in accuracy between tests is small and choice of test should be guided by the malaria epidemiology of a site combined with the cost and availability of the test. The HRP-2 antigen persists even after effective treatment and so pLDH tests should be chosen for treatment failure detection.

The full text of the Cochrane Review is available in *The Cochrane Library*: Abba K, Deeks JJ, Olliaro PL, Naing CM, Jackson SM, Takwoingi Y, Donegan S, Garner P. Rapid diagnostic tests for diagnosing uncomplicated *P. falciparum* malaria in endemic countries. *Cochrane Database of Systematic Reviews* 2011, Issue 7. Art. No.: CD008122. DOI: 10.1002/14651858.CD008122.pub2.

Commentary: Rapid diagnostic tests for diagnosing uncomplicated *Plasmodium falciparum* malaria in endemic countries (Review)

Emmanuel Bottieau,[1] Jan Jacobs[1] and Jean B Nachega[2,3]*

[1]Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium, [2]Department of Medicine and Centre for Infectious Diseases, Stellenbosch University Faculty of Health Sciences, Cape Town, South Africa and [3]Departments of Epidemiology and International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

*Corresponding author. Department of Medicine, Faculty of Health Sciences, University of Stellenbosch, PO Box 19063, Tygerberg 7505, South Africa. E-mail: jnachega@sun.ac.za

Major progress in prevention, diagnosis and treatment, as well as growing international financing and renewed global political commitment have had an impact on the prevalence of malaria.[1] However, global malaria deaths (almost exclusively attributable to *Plasmodium falciparum*) still reached 1 238 000 (929 000–1 685 000) in 2010,[2] far beyond the World Health Organization (WHO) estimates,[1] the difference being explained by the large underestimation of malaria mortality, in particular in children aged >5 years and in adults.

Early, prompt and accurate diagnosis of malaria, followed by adequate treatment, reduce morbidity and mortality. Microscopy is technically demanding, so simple Rapid diagnostic tests (RDTs) are potentially important. These tests mainly detect histidine-rich protein-2 (HRP-2) or plasmodium lactate dehydrogenase (pLDH) specific to *P. falciparum* (Pf), alone or in combination with other antigens. Since any patient suspected of malaria should be tested either by microscopy or RDT before treatment,[3] the systematic review of Abba *et al.* assessing the performances of current RDTs in diagnosing *P. falciparum* malaria is most welcome. After having analysed 111 test evaluations in 74 unique studies assessing 21 different RDT brands and 60 396 RDT results, the conclusion is straightforward: performance of RDTs is such nowadays that it may replace microscopy for patient care. Readers are also elegantly provided tables for interpreting RDT performances in different epidemiological scenarios.

The review findings are particularly robust for the RDTs targeting HRP-2 or Pf-pLDH alone (of note, pLDH, if not clearly defined, may also refer to pan-pLDH, common to all *Plasmodium* species). As acknowledged by the authors, the number of studies evaluating combined RDTs is much smaller, resulting in large 95% confidence intervals and unsatisfactory diagnostic accuracy when considering the lowest ranges. Such RDTs are more expensive and also more difficult to interpret by less educated caregivers. Another limitation is that the rare, but worrying prozone phenomenon (false-negative or low results in case of high parasite density) has not been explored.[4] According to a study published after January 2010, prozone only affects HRP-2-based RDTs at variable frequency and intensity but may account for up to 1% of false-negative results in patients with *P. falciparum* malaria (unfortunately those with hyperparasitaemia, at highest risk of complication).[4] Finally, no RDT type was clearly superior to another in terms of sensitivity, but HRP-2-based RDTs were less specific. The long persistence of HRP-2 after parasite clearance is indeed of concern in areas of high malaria transmission.[5] Side-to-side comparisons of both types of RDTs are now required in different epidemiological settings, to refine their respective positioning. No universal 'one-size-fits-all' RDT is to be expected for all variable and evolving malaria contexts. Meanwhile, the authors must be congratulated for this impressive piece of work that provides reassurance for the caregivers and policy makers of the many endemic countries where RDTs have already been deployed towards the most peripheral health facilities.

References

1 World Health Organization. World Malaria Report 2010. Geneva: WHO, 2012.
2 Murray CJ, Rosenfeld LC, Lim SS *et al*. Global malaria mortality between 1980 and 2010: a systematic analysis. *Lancet* 2012;**379:**413–31.
3 World Health Organization. *Guidelines for the Treatment of Malaria*. WHO: Geneva, 2010.
4 Gillet P, Scheirlinck A, Stokx J *et al*. Prozone in malaria rapid diagnostics tests: how many cases are missed? *Malar J* 2011;**10:**166.
5 Bisoffi Z, Sirima SB, Menten J *et al*. Accuracy of a rapid diagnostic test on the diagnosis of malaria infection and of malaria-attributable fever during low and high transmission season in Burkina Faso. *Malar J* 2010;**9:**192.

Approach to conducting Cochrane Diagnostic Test Accuracy Reviews

Mariska Leeflang

Clinical Epidemiology and Biostatistics, Academic Medical Center, Amsterdam Room J1b-209. E-mail: m.m.leeflang@amc.uva.nl

Cochrane diagnostic test accuracy (DTA) reviews assess the accuracy of diagnostic medical tests. The accuracy of a test determines how well a test is able to differentiate between people with and without the target condition. Accuracy is often expressed in sensitivity (the proportion of persons with the target condition who test positive) and specificity (the proportion of persons without the target condition who test negative).

As for all systematic reviews, a DTA review starts with a research question. This question leads the rest of the review and is of utmost importance. Most questions will be comparative questions: is MRI better than CT to detect stroke in elderly