A systematic review and meta-analysis of the diagnostic accuracy of rapid immunochromatographic assays for the detection of dengue virus IgM antibodies during acute infection


CRD summary
This review found that rapid immunochromatographic tests can be used to rule in and out infection with dengue virus, but are more accurate when samples are collected later in the acute phase of infection. These findings are supported by the results presented, but should be interpreted with caution given the limitations in the searches and the presence of significant variability between studies.

Authors' objectives
To evaluate the accuracy of rapid dengue virus diagnostic assays and to investigate sources of heterogeneity between studies.

Searching
MEDLINE (1966 to March 2004), EMBASE (1994 to March 2004), the Cochrane Library, Web of Science and Scirus were searched. The search terms were reported and included a diagnostic filter. No language restrictions were applied. The reference lists of selected studies were screened for additional relevant studies.

Study selection
Study designs of evaluations included in the review
No inclusion criteria relating to the study design were specified. The included studies used either a diagnostic cohort or diagnostic case-control design.

Specific interventions included in the review
Studies that evaluated rapid (60 minutes or less) point of care immunochromatographic tests (ICTs) for the detection of dengue virus immunoglobulin M (IgM) antibodies were eligible for inclusion. Assays limited to the detection of IgG and assays taking longer than 60 minutes to perform were excluded. The studies had to include sufficient study samples (unclear what was considered sufficient) and a complete description of the samples so that the timing of sample collection could be determined. All included studies evaluated the PanBio ICT.

Reference standard test against which the new test was compared
Studies that used an inappropriate reference standard, including in-house' assays for which the diagnostic accuracy had not been previously established, were excluded. Studies in which not all of the study samples received the reference standard, or which used multiple reference assays, were excluded. The reference standards used in the included studies were Panbio Duo ELISA, Panbio IgM ELISA, MRL IgM ELISA, AFRIMS MAC-ELISA and HAI.

Participants included in the review
Studies that evaluated individuals with dengue fever, dengue shock syndrome or dengue haemorrhagic fever upon hospital admission or during the acute phase of infection were eligible for inclusion. Studies that included an inappropriate study population, such as only individuals undergoing convalescence, were excluded. Studies of samples obtained from South-East Asia, India and the Americas were conducted. Studies included patients with both early and late acute infection; none of the studies described the severity of infection.

Outcomes assessed in the review
Studies with errors or inconsistencies in the published study data or that barred indeterminate results were excluded. The outcomes reported in the review were the sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratios.
How were decisions on the relevance of primary studies made?
Abstracts of identified studies were printed and full-text articles of potentially relevant studies were obtained. It was unclear how many reviewers assessed studies for relevance.

Assessment of study quality
Two reviewers assessed the quality of the included studies using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool. It was unclear whether this was done independently. The studies were assigned a score out of 14 according to the number of QUADAS items fulfilled.

Data extraction
Two reviewers independently extracted the data from the included studies using a standardised form. Any disagreements were resolved through mediation. For studies that included multiple data sets, only IgM results for admission sera that were compared with a valid reference standard were extracted. Infection status (primary or secondary) was assigned using criteria defined in individual studies. The data were extracted as 2x2 tables of test performance. The sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratios were calculated with 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
Measures of diagnostic accuracy were pooled. A fixed-effect model was used if heterogeneity was not considered to be significant, otherwise a random-effects model was used. Summary receiver operating characteristic curves were produced and the area under the curve was estimated.

How were differences between studies investigated?
Chi-squared and I-squared statistics were calculated in order to assess heterogeneity. Significant heterogeneity was considered to be present if the chi-squared result was a p-value of less than 0.10. Data were stratified into early acute (up to 7 days after onset of symptoms) and late acute (7 to 10 days after onset of symptoms); subgroup analysis was carried out according to the type of reference test used, sample collection time, study design and infection status.

Results of the review
Eleven studies (n=912) were included: 5 prospective cohort studies and 6 case-control studies.

The proportion of QUADAS items fulfilled by the included studies ranged from 43 to 79%.

The sensitivity ranged from 45 to 100% and specificity from 57 to 100%. The pooled sensitivity and pooled specificity were 86% (95% CI: 74, 92) and 88% (95% CI: 78, 94), respectively. There was significant heterogeneity (p<0.1) and I-squared was 97.7.

Heterogeneity remained after grouping according to reference standard, sample collection timing, study design and infection status. Accuracy was higher for late acute infection samples than for early acute samples.

Cost information
No

Authors' conclusions
Dengue ICT is a potentially helpful test when performed under specified conditions.

CRD commentary
The review addressed a focused objective. However, inclusion criteria were not reported and had to be deduced from the exclusion criteria which were largely based on the quality assessment. The literature search was limited by the inclusion of a diagnostic filter, only a small number of databases were searched, and no attempts to locate unpublished studies were made. Relevant studies may therefore have been missed. A detailed quality assessment was carried out and the results of this used as a basis for including studies in the review. However, the results of the quality assessment for the individual included studies were not reported, although other relevant details were summarised in a table. Some details of the review process were described and these included appropriate steps to minimise bias. However, it was unclear how studies were selected for inclusion in the review and whether the quality assessment was conducted independently.

The methods used to pool the studies were appropriate and heterogeneity was investigated. The inclusion of a summary receiver operating characteristic plot would have helped in the interpretation of the results. The authors’ conclusions should be interpreted with some degree of caution given the limitations in the literature search and the significant heterogeneity between studies, which remained even after stratification.

Implications of the review for practice and research
Practice: The authors states 'ICT can both rule in and rule out disease but is more accurate when samples are collected later in the acute phase of infection'.

Research: The authors stated the need for additional diagnostic accuracy studies of other dengue ICTs using a standardised, agreed methodology performed by independent bodies.

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