Accuracy of rapid and point-of-care screening tests for hepatitis C: a systematic review and meta-analysis

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CRD summary
This review concluded that rapid diagnostic tests and point-of-care tests may have been useful in expanding screening of hepatitis C. Despite some uncertainty about the analyses, the overall conclusions are likely to be reliable. Test accuracy may be overestimated to some degree, primarily due to the lack of blinding within the primary studies.

Authors' objectives
To evaluate the diagnostic performance of rapid diagnostic tests and point-of-care tests to screen for hepatitis C.

Searching
The authors searched PubMed, EMBASE, BIOSIS and Web of Science without language restrictions from 1992 to 1st March 2012. Search terms were reported. Bibliographies of included articles were also screened for additional studies.

Study selection
To be eligible, studies had to evaluate the diagnostic accuracy of available rapid diagnostic tests and point-of-care tests to screen for hepatitis C in oral fluid, whole blood, serum or plasma specimens. Tests that were easy to use, were robust at high temperatures and had a shelf life more than six months were considered point-of-care tests. Rapid diagnostic tests were those that required sample processing and refrigerators for storage. Both types of test had to be performed in less than 30 minutes. Studies could be conducted in any country and study setting. Participants were adults (aged 18 or over) with any risk profile. All study designs were acceptable as long as there were sufficient data to create a 2x2 table of test performance. Prevalence studies were excluded as were studies of the accuracy of laboratory-based tests. Studies with missing information about the index test under evaluation, manufacturer reports and package inserts were all excluded.

Fifty-eight percent of the studies were conducted in developing settings. Thirteen different tests were included in the review but all were antibody-based.

Two reviewers independently screened the studies for eligibility.

Assessment of study quality
The authors used QUADAS-2 and STARD to assess quality.

Two reviewers independently assessed the quality of the included studies with disagreements resolved by reference to a third reviewer.

Data extraction
Date were extracted that related to 2x2 tables of test performance from which sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratios were calculated.

Two reviewers independently extracted data with a pre-piloted form with disagreements resolved by reference to a third reviewer.

Methods of synthesis
Studies were grouped according to the type of test and whether the sample was serum, plasma, whole blood or oral fluid. Pooled estimates of sensitivity and specificity with 95% confidence intervals (CI) were derived from a bivariate random-effects model. Studies were combined using meta-analysis based on these groupings to generate pooled sensitivities and specificities. One study with a sensitivity of 0% and a specificity of 100% was excluded from the quantitative analysis. A positive likelihood ratio of 5 and a negative likelihood ratios of 0.2 was used to determine an informative test.
Results of the review

Nineteen studies were included in the review (at least 12,657 participants). Twelve were cross-sectional and seven were case-control studies. Sample size ranged from 60 to 2,754 participants. All studies avoided differential and partial verification bias but only three reported blinding of the test interpreters. The quality of study reporting ranged from poor to good (STARD scores from 8 to 20 out of 25). Nine of 19 studies used the ideal reference standard as recommended by the Centers for Disease Control and Prevention.

For rapid diagnostic tests of serum or plasma (10 data sets) the pooled sensitivity was 98.4% (95% CI, 88.9 to 99.8) and the pooled specificity was 98.6% (95% CI, 94.9 to 99.6). For point-of-care tests of serum or plasma (11 data sets) the pooled sensitivity was 98.9% (95% CI, 96.8 to 99.6) and the pooled specificity was 99.7% (95% CI, 99.3 to 99.9). For point-of-care tests of whole blood or finger-stick blood (10 data sets) the pooled sensitivity was 98.9% (95% CI, 94.5 to 99.8) and the pooled specificity was 99.5% (95% CI, 97.5 to 99.9). For point-of-care tests of oral fluids (seven data sets) the pooled sensitivity was 97.1% (95% CI, 94.7 to 98.4) and the pooled specificity was 98.2% (95% CI, 92.2 to 99.6).

Authors’ conclusions

Given their accuracy, convenience and quick turnaround time, rapid diagnostic tests and point-of-care tests may have been useful in expanding screening of hepatitis C. Point-of-care tests of blood (serum, plasma or whole blood) have the highest accuracy, followed by rapid diagnostic tests of serum or plasma and point-of-care tests of oral fluids.

CRD commentary

This review was based on defined inclusion criteria and underpinned by a search of several databases. Unpublished studies did not appear to be included, which opened the review up to publication bias. Quality was assessed using appropriate tools, but results were not reported in full. A large proportion of the studies did not report blinding and several were subject to selection bias. Two reviewers were involved in selecting studies, data extraction and quality assessment which helped minimise bias and error. Grouping of the studies appeared to have been appropriate.

The authors stated that they used a bivariate model to produce the summary estimates of sensitivity and specificity. However, the pooled estimates of the likelihood ratios did not seem to be derived from these. Therefore, it was unclear whether frequentist meta-analytical techniques, or robust summary receiver operating characteristic curve analyses (which maintain the within-study relationship between the sensitivity and specificity) were used to derive these estimates. Given the heterogeneity of the included studies, the reliability and generalisability of estimates of sensitivity and specificity produced in separate analyses would be uncertain. In addition, results of investigations into between-study heterogeneity were not reported, and it was unclear whether any covariates were included in the bivariate analyses. Although they have been graded by the authors, all of the tests had positive likelihood ratio of over 50, and negative likelihood ratio of 0.3 or lower, so were informative.

Despite some uncertainty regarding the analyses, the overall conclusions are likely to be reliable, although test accuracy may be overestimated to some degree, primarily due to the lack of blinding within the primary studies.

Implications of the review for practice and research

Practice: The authors stated that the many advantages offered by rapid diagnostic tests and point-of-care tests could be optimised by integrating them into usual care pathways in outpatient clinics, emergency departments and public health clinics. The tests could play a role in the screening of marginalised and at-risk populations and in settings where hepatitis C was endemic.

Research: The authors stated that future diagnostic accuracy studies require a standardised reference standard. Future studies should be stratified by co-infection to ascertain the diagnostic accuracy of these tests in the presence of co-infection. Further research was needed on the effect of hepatitis C genotype. There should be replication of trials that received industry funding. More research was needed linking screening with follow-up especially in hard to reach populations and in low resource settings. Outcomes other than diagnostic accuracy need to be investigated, including patient-centred outcomes, operational outcomes and cost.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.