Rapid diagnostic testing for seasonal influenza: an evidence-based review and comparison with unaided clinical diagnosis

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CRD summary
This review concluded that rapid flu tests improved seasonal influenza diagnostic specificity over clinical diagnosis alone and affected clinical decision making. Weaknesses in the analytical methods and reporting of the review mean that these conclusions should be viewed with caution.

Authors’ objectives
To determine the age-specific performance characteristics of QuickVue rapid flu tests (QuickVue®, Quidel Corporation, CA) and clinical diagnosis of influenza-like illness in seasonal influenza.

Searching
PubMed, the Cochrane Library, BMJ Clinical Evidence, Surveillance and Epidemiology and End Results (SEER), the World Health Organization website, and the Agency for Healthcare Research and Quality website were searched for articles published in English from 1984 to 2009. Search terms were reported. Bibliographies of included studies were screened for additional articles.

Study selection
Studies of any design, conducted in adults or children presenting with influenza-like illness that reporting sufficient data to calculate sensitivity and specificity of rapid flu tests or clinical diagnosis, and that reported clinical outcomes associated with rapid flu test use, were eligible for inclusion. Included studies had to describe a defined population age group and have an unrestricted geographical territory. Diagnosis had to be confirmed using specimens obtained by nasal or nasopharyngeal swab, or nasopharyngeal aspirate or wash and viral culture PCR immunofluorescence or serology in most patients. Studies that compared two or more rapid flu tests were only included if the same specimen processing methods were used for both tests. Studies that indicated lack of presentation or specimen collection within two to four days of symptom onset were excluded. Test accuracy studies based on frozen specimens were also excluded.

Included participants ranged from two weeks to 94 years of age.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The methodological quality was assessed using US Preventive Services Task Force (USPSTF) criteria including: relevance and availability of test in primary care; adequate description of the test; use of an acceptable reference standard, performed regardless of index test results; reference standard interpreted independently of index test; appropriate handling of indeterminate test results; participant spectrum; and sample size.

The authors did not state how many reviewers assessed methodological quality.

Data extraction
All included studies appeared to have been test accuracy studies. Data were extracted on the numbers of true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) test results for each included study and test (rapid flu tests and clinical diagnosis). Qualitative data on the impact of rapid flu test on physician-chosen patient management (increase/decrease in diagnostic testing, antibiotic use, use of antiviral medication and emergency department length of stay) were also extracted, where available.

The authors did not state how many reviewers performed the data extraction.
Methods of synthesis
Studies were stratified by participant age as older (15 years and older), younger (younger than 15 years), and overall (all ages). Pooled estimates of sensitivity and specificity, with 95% confidence intervals (CIs), were calculated for each test (QuickVue® rapid flu tests and clinical diagnosis) and participant group. Pooled estimates were calculated using both fixed-effect and random-effects models. Between-study heterogeneity was assessed using $I^2$.

Individual study results for both tests were plotted in receiver operating characteristic (ROC) space and a summary curve was fitted for clinical diagnosis.

Results of the review
Sixteen studies (n=15,629 participants) were included in the review.

For all ages combined, the sensitivity and specificity estimates for QuickVue rapid flu tests (19 studies, n=5,502 participants) were 72% (95% CI 62 to 81) and 96% (95% CI 93 to 97). The sensitivity and specificity estimates for clinical diagnosis (16 studies, n=10,316 participants) were 65% (95% CI 55 to 74) and 67% (95% CI 57 to 76).

For the older age group, the sensitivity and specificity estimates for QuickVue rapid flu tests (five studies, n=1,683 participants) were 61% (95% CI 36 to 81) and 96% (95% CI 94 to 98). The sensitivity and specificity estimates for clinical diagnosis (11 studies, n=6,705 participants) were 64% (95% CI 51 to 75) and 68% (95% CI 57 to 77).

For the younger age group, the sensitivity and specificity estimates for QuickVue rapid flu tests (14 studies, n=3,819 participants) were 76% (95% CI 65 to 85) and 95% (95% CI 92 to 98). The sensitivity and specificity estimates for clinical diagnosis (five studies, n=3,611 participants) were 69% (95% CI 44 to 87) and 63% (95% CI 31 to 87).

The only estimate not to show substantial heterogeneity was that for QuickVue rapid flu tests in the older age group.

The authors stated that three studies comparing performance of two or more rapid flu tests did not suggest any difference in performance between rapid flu tests. However, only data for QuickVue tests were reported.

Ten studies reported outcomes related to physician-chosen patient management. In these studies, rapid flu test use in patients presenting with influenza-like illness led to reduced diagnostic testing, antibiotic use and emergency department length of stay; they increased antiviral prescribing.

Authors’ conclusions
Use of rapid flu tests improved seasonal influenza diagnostic specificity above that based on unaided clinical diagnosis irrespective of the broadness of clinical diagnostic criteria, and affected clinical decision-making.

CRD commentary
The review objective was clearly stated and appropriate inclusion criteria were defined. A number of sources were searched for relevant studies, but the restriction to published English language studies raised the possibility of publication and/or language bias. The use of methodological terms to identify test accuracy studies could have further reduced search sensitivity. It was not clear whether any measures were taken to minimise error and/or bias in the review process.

Although the authors stated that they assessed the methodological quality of included studies, no results of this assessment were reported. Consequently, the reliability of both individual study and review results is uncertain. The generation of pooled estimates of sensitivity and specificity, using a random effects model rather than a summary ROC model, was of questionable validity, given the substantial heterogeneity present in most data sets. An receiver operating characteristic plot for QuickVue rapid flu tests and clinical diagnosis appeared to indicate improved accuracy of diagnosis using QuickVue. However, no statistical comparisons were reported for the performance of rapid flu tests and clinical diagnosis, and no distinction was made between data derived from direct comparisons between the two tests in the same patient group and indirect comparisons derived from different studies (most data were derived from indirect comparisons).
Overall, methodological limitations and weaknesses in the reporting of the review mean that the authors' conclusions should be viewed cautiously.

All of the review authors disclosed financial and employment links with the Aequitas Group/Quidel Corporation (manufacturers of QuickVue rapid flu tests and funders of the review).

Implications of the review for practice and research

Practice: The authors stated that there may be benefits to using rapid flu tests outside the peak influenza season.

Research: The authors stated that further comparative studies of the performance of rapid flu tests and unaided clinical diagnosis are needed help to develop specific guidelines for rapid flu test use and improve patient management. They also recommended a detailed cost-effectiveness analysis, based on the results of their review.

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