Does this patient have influenza?

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CRD summary
This review attempted to quantify the discriminatory ability of the clinical signs and symptoms used to diagnose influenza. The authors stated that no single clinical finding or combination of the findings was found to be capable of ruling in or ruling out disease. The pooling of diverse data and the lack of methodological details make the reliability of the results uncertain.

Authors' objectives
To assess the precision and accuracy of symptoms and signs for the diagnosis of influenza.

Searching
MEDLINE was searched from 1966 to September 2004, limiting the search to the period prior to the SARS (severe acute respiratory syndrome) outbreak; a further search (from 1996 to October 2004) was conducted for English language articles on rapid diagnostic kits for influenza. The search terms for both searches were reported. The bibliographies of retrieved, English language review articles and one systematic review were checked for further relevant articles. Data from manufacturers were also sought. Unpublished primary data were not sought during either search.

Study selection
Study designs of evaluations included in the review
Prospective diagnostic cohort studies, randomised controlled trials (RCTs) and meta-analyses were eligible for inclusion.

Specific interventions included in the review
Studies of the diagnosis of influenza based on clinical signs and symptoms were eligible for inclusion. The signs and symptoms evaluated included: fever, chills, sore throat, cough, headache, myalgia, malaise, sneezing and nasal congestion.

Reference standard test against which the new test was compared
The included studies had to establish the diagnosis of influenza type A or B using culture, a 4-fold increase in diagnostic antibody titre, polymerase chain reaction, or immunofluorescent antibody. Each of the six included studies used a different reference standard technique.

Participants included in the review
No inclusion criteria were specified for the study participants. The included studies were of participants of all ages (range: 1 to at least 90 years).

Outcomes assessed in the review
No inclusion criteria were specified for the diagnostic outcome measures. The sensitivity, specificity, positive and negative likelihood ratios (LRs) and diagnostic odds ratio (DOR) were reported, by symptom, for the included studies.

How were decisions on the relevance of primary studies made?
The authors did not clearly state how decisions on the relevance of the primary studies were made. Two reviewers independently assessed the final set of 17 studies for inclusion. Any disagreements were resolved by consensus.

Assessment of study quality
A limited grading of study quality was performed. This assessed the use of an appropriate reference standard, the
blinding of investigators, sample size and consecutive recruitment of participants. Two reviewers independently assessed study quality. Any disagreements were resolved by consensus.

Data extraction
Two reviewers independently extracted data to calculate diagnostic accuracy parameters and influenza prevalence from the included studies. Any disagreements were resolved by consensus.

Methods of synthesis
How were the studies combined?
Summary LRs and DORs were estimated for individual components of history and physical examination, using a random-effects model.

How were differences between studies investigated?
The heterogeneity of the LRs was tested using the Q-statistic. Differences between the studies were also discussed in the text.

Results of the review
Six studies were included: one retrospective pooled analysis of clinical trials (n=3,744), one RCT of influenza vaccine (n=1,838) and four prospective diagnostic cohort studies (n=1,582). Six further studies evaluated rapid test kits for the diagnosis of influenza: five prospective diagnostic cohort studies (n=1,089) and one prospective/retrospective cohort (n=33).

None of the included studies assessed the precision of signs or symptoms.

No single sign or symptom had a positive LR high enough to rule in influenza, or a negative LR low enough to rule it out.

In an unselected population, the absence of fever (LR 0.40, 95% confidence interval, CI: 0.25, 0.66), cough (LR 0.42, 95% CI: 0.31, 0.57), or nasal congestion (LR 0.49, 95% CI: 0.42, 0.59) decreased the likelihood of influenza. These were the only findings with an LR of less than 0.5.

In studies limited to patients aged 60 years and older, the combination of fever, cough and acute symptom onset (LR 5.4, 95% CI: 3.8, 7.7), fever and cough (LR 5.0, 95% CI: 3.5, 6.9), fever alone (LR 3.8, 95% CI: 2.8, 5.0), malaise (LR 2.6, 95% CI: 2.2, 3.1) and chills (LR 2.6, 95% CI: 2.0, 3.2) increased the likelihood of influenza. The presence of sneezing in these patients made influenza less likely (LR 0.47, 95% CI: 0.24, 0.92).

The only study to compare four rapid tests (Directigen Flu A, Zstat Flu A/B, QuickVue Influenza Test A/B and Flu OIA A/B) with a reference standard (viral culture) reported that, overall, the tests were similar, with a summary positive LR of 4.7 (95% CI: 3.6, 6.2) and a negative LR of 0.06 (95% CI: 0.03, 0.12).

Authors' conclusions
Clinical findings identify patients with influenza-like illness but are not particularly useful for confirming or excluding the diagnosis of influenza.

CRD commentary
The review addressed a clearly stated research question using an appropriate, though not comprehensive, set of inclusion criteria. The literature search was limited and unpublished data were not sought; it is therefore possible that relevant data were missed. In addition, the authors did not investigate publication bias. The review methodology was adequately described and appropriate measures were taken to avoid the introduction of bias and error during the review process. A limited grading of study quality was performed, the results of which were reported but not considered in the analysis. Other details of the included studies were tabulated clearly. The pooling of the demonstrably heterogeneous
Implications of the review for practice and research
Practice: The authors stated that no specific symptom or combination of symptoms is diagnostic of influenza. They further stated that clinicians should view signs and symptoms of the disease in the context of current surveillance data.

Research: The authors did not state any implications for further research.

Bibliographic details

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Other publications of related interest
This additional published commentary may also be of interest. Carrier J. Review: fever and cough are the most accurate single tests for diagnosing influenza. Evid Based Nurs 2005;8:121.

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Record Status
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.