# Critical Review Form

## Diagnostic Test

Performance Characteristics of Clinical Diagnosis, a Clinical Decision Rule, and a Rapid Influenza Test in the Detection of Influenza Infection in a Community Sample of Adults, *Annals EM* 2005; 46:412-419

**Objective:** **To assess the test characteristics of the "cough and fever" clinical prediction rule compared with clinician judgment and rapid influenza testing using a more unselected community-based patient population seeking care for acute respiratory illness "defined as the development of a new illness within the past 3 weeks associated with cough, sinus pain, nasal congestion, rhinorrhea, sore throat or fever." (p 413)**

**Methods:** **Prospective convenience sampling of consecutive adults (> 18 years) presenting to UCSF ED or Urgent Care ambulatory clinic with the above symptoms during influenza season from January – March 2002. Exclusion criteria included pregnancy, systemic inflammatory disorder, acute coronary syndrome cancer, AIDS, or current antibiotic use. Enrollment was 6 days/week from 9am-5pm.**

**Research assistants collected specimens and completed standardized encounter forms with patient demographics. The Quidel QuickVue rapid influenza test was performed by trained research assistants according to manufacturer's recommendations and the Gold Standard reverse transcription polymerase chain reaction (rt-PCR) was obtained on all subjects visualized on ethidium bromide-stained agarose gels with UV illumination from frozen specimens stored at -70°C.**

**The primary outcome measure was the detection of influenza A or B using rt-PCR. Secondary outcomes included clinician judgment for influenza blinded to QuickVue results "shortly after they had completed the patient's ED visit". Another outcome was the accuracy of Monto's previously derived CDR of cough and fever correlating positively with influenza as the etiology on a select subset of patients (Monto AS, et al, *Arch IM* 2000; 160:3243-3247).**

**Univariate analysis was performed with SAS software using chi-squared, t-tests or Wilcoxan rank sum measures as appropriate for data sets. To derive the statistical significance of comparisons between clinician judgment, Monto's CDR and the rapid influenza test, McNemar's test of proportions was used. Multivariable**

**logistic regression analysis was used to asses the impact of illness duration ( >48 hours, <48 hours) on these 3 models of diagnosing influenza. No power calculation was reported.**

| Guide | | Comments |
|---|---|---|
| **I.** | **Are the results valid?** | |
| **A.** | **Did clinicians face diagnostic uncertainty?** | Yes – highly generalized group of subjects presenting with up to 3 weeks of symptoms and myriad complaints of uncertain etiology. |
| **B.** | **Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?** | Yes, "microbiologists were blinded to the clinical information, as well as to the result of the rapid influenza test" (p.414). |
| **C.** | **Did the results of the test being evaluated influence the decision to perform the gold standard?** | No – all subjects had the Gold Standard rt PCR performed. |
| **II.** | **What are the results?** | |

| A. | **What likelihood ratios were associated with the range of possible test results?** |
|---|---|
| | |

- 258 / 405 eligible subjects were enrolled with the only demographic differences noted between non-influenza and influenza subjects being a lower proportion of Hispanic subjects and shorter illness duration (6.7 d vs. 4.8 d) among those with influenza (Table 1 p.414)
- Influenza prevalence was 21%. This allows physicians to estimate a pre-test probability when faced with similar patients during flu season.
- 25% of those with Influenza presented in <48º compared with 16% of those without Influenza.
- Those with Influenza were more likely to report fever, swales muscle pain and sinus pain while those without Influenza more commonly complained of throat swelling.
- See Table 1 (below) summarizing three models of diagnosing Influenza.
- There was no statistically significant difference between clinician judgment and the decision rule or the rapid influenza test (p=0.1 by McNemar's test).
- When stratified by duration of illness, clinician judgment improve for symptoms <48 hours (see below) (p=0.017).

| | Sen | Spec | LR+ | LR- |
|---|---|---|---|---|
| Symptoms < 48° | 67% | 96% | 17.3 | 0.4 |
| Symptoms > 48º | 17% | 92% | 2.0 | 0.9 |

| | | |
|---|---|---|
| | | • Non-statistically significant sensitivity decreases/specificity increases were noted for the CDR and the QuickVue rapid test when symptoms present > 48 hours. |

| III. | How can I apply the results to patient care? | |
|---|---|---|
| **A.** | **Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?** | Probably since the current study represents a loss select, more heterogeneous population of acute upper respiratory illness sufferers presenting to ED's like BJH. |
| **B.** | **Are the results applicable to the patients in my practice?** | To the adult patients who are immunocompetent at BJH. Probably not applicable to pediatric populations. |
| **C.** | **Will the results change my management strategy?** | Yes. The results will provide an estimate of influenza prevalence during a typical flue season or non-select adults presenting to the ED for diagnosis and management of upper respiratory complaints. Among all – comers, QuickVue offers superior diagnostic performance to either Monto's CDR on clinical gestalt, but <u>when stratified by symptom duration <48° clinical gestalt is superior</u>. |
| **D.** | **Will patients be better off as a result of the test?** | Yes, if unnecessary ED testing (& concomitant delays) can be avoided in evaluating upper respiratory complaints in adults without sacrificing diagnostic accuracy. |

**Limitations:**

1) **No power analysis – did the investigators recruit a sufficiently large sample to detect a difference if one truly exists?**
2) **No description of experience level of clinicians. Clinical gestalt likely varies by prior experiences underlying biases and thought processes and confounding influences.**
3) **Investigators did not ascertain immunization status.**
4) **C-reactive protein basis of study population may have skewed results (selections bias), although only 3% excluded by these criteria so unlikely.**
5) **Reliance on rt-PCR as Gold Standard (rather than viral cultures) may result in false positives (from previously amplified DNA) which would artificially depress the sensitivity of other tests like QuickVue, Monto's CDR and clinical gestalt.**

**Bottom Line:**

**In a non-select group of adults with up to 3 weeks of upper respiratory complaints at one hospital's ED, clinical clinical gestalt is equal to Monto's CDR or QuickVue rapid influenza testing in the diagnosis of Influenza, although QuickVue LR+ is far superior (LR+ 28.2 for QuickVue vs. 3.8 for gestalt or 5.1 for Monto's CDR). Clinical gestalt is improved when symptoms have been present for <48 hours (LR+ 17.3). QuickVue (and other POCT) may play a role if a positive test would obviate the need for further diagnostic testing, although formal cost-effectiveness trials will need to confirm this observation.**

**Table 1**
**Test Characteristics of Three Decision Models for ED Diagnosis of Influenza on Unselected Adult Patients**

| Diagnostic Model | Sensitivity (95% CI) | Specificity (95% CI) | $LR^+$ (95% CI) | $LR^-$ (95% CI) |
|---|---|---|---|---|
| **Clinician Judgment** | 29% (18-43%) | 92% (87-95%) | 3.8 (1.9-7.5) | 0.8 (0.6-0.9) |
| **Monto's CDR** | 40% (27-54%) | 92% (87-95%) | 5.1 (2.7-9.6) | 0.7 (0.5-0.8) |
| **QuickVue Rapid Influenza Test** | 33% (22-47%) | 98% (96-99.7%) | 28.2 (6.7-118.2) | 0.7 (0.6-0.8) |