# Critical Review Form

## Diagnostic Test

Effect of Point-of-Care Influenza Testing on Management of Febrile Children, *Acad EM* 2006; 13:1259-1268

**Objectives:** **"To determine the effect of point-of-care testing (POCT) for influenza on the physician management of febrile children who are at risk for serious bacterial illness (SBI) and present to a pediatric ED during an influenza outbreak." (p.1260)**

**Methods:** **Prospective, quasi-randomized (on alternate days), controlled trial at Cincinnati Children's Hospital of children age 2-3 months with temperature ≥38°C (rectal, oral, or ancillary) or 3-24 months ≥39ºC (in ED or at home) presenting between 12p – 12a during one of two Infection Control labeled Influenza outbreaks (1/27/03 – 3/31/03 or 12/8/03 – 1/29/04). Exclusion criteria included chronic lung disease congenital heart disease, immunocompromised state and critical acuity level, medical contraindication to nasal swales or previous enrollment. "The method of testing POCT or Standard Testing (ST) was strictly alternated by day". (p.1261). POCT was QuickVue Influenza Test (manufactured by Quidel who sponsored the trial) with results available to treating EM clinicians within 30 minutes and prior to other ancillary testing. Standard Testing, on the other hand, was QuickVue batched twice daily and if patient was still in ED when batch sent, testing of that specimen was delayed to next batch to ensure results were not available to clinicians while the patient was still in the ED.**

**The primary outcome measure was blood culture ordering. Secondary outcomes included the ordering of CBC, urinalysis, urine culture, lumbar puncture, chest radiograph, and antibiotics. Finally, ED length-of-stay, visit-associated costs, admissions and repeat ED visits were also evaluated.**

**Data analysis consisted of univariate statistical computation for variables followed by logistics regression to measure the association of blood culture ordering with the method of testing (POCT versus ST) and the Influenza test result while controlling for confounding variables. The results of the logistic regression were reported as odds of test being performed in POCT-positive and patient relative to POCT-negative patient (or $ST^+$ and relative to $ST^-$ patient). Based on the previous years blood culture order rate of 40%, the authors power calculation was 80% powered with α=0.05 if the $POCT^+$ group demonstrated a 50% reduction (to 20%) blood culture ordering rate, although their post-hoc analysis demonstrated only 22% power based on the actual ordering rate.**

| Guide | | Comments |
|---|---|---|
| **I.** | **Are the results valid?** | |
| **A.** | **Did clinicians face diagnostic uncertainty?** | Yes – febrile children <2 yrs old without a clear etiology of fever. Uncertain how many had focused symptoms, but few had alternative bacterial etiology identified in either group. |
| **B.** | **Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?** | No. Only one test (QuickVue) was performed in either group and not confirmed by any other objective test. |
| **C.** | **Did the results of the test being evaluated influence the decision to perform the gold standard?** | No Gold Standard was applied. Importance since QuickVue's sensitivity is 74% so some cases of influenza may have been missed. |
| **II.** | **What are the results?** | (See below) |

| | | |
|---|---|---|
| **A.** | **What likelihood ratios were associated with the range of possible test results?** | Here are the results we can deduce from this study.<br>• 700 subjects were enrolled representing 91% of eligible subjects.<br>• 205/700 (29.3%) Influenza-positive rate provides estimate of pre-test probability.<br>• No significant differences were demonstrated between POCT and ST groups with respect to lab or CXR ordering, antibiotic use, ED LOS or visit-associated costs.<br>• However, when broken down to $POCT^+$, $POCT^-$, $ST^+$, and $ST^-$ sub-groups, fewer blood cultures were ordered when either test was positive, but a POCT-positive result was associated with a further reduction that approached statistical significance. Numerically, this is expressed in Table 1 below.<br>• To further quantitate the diminished testing in $POCT^+$ subset, the authors logistic regression model permitted calculation of adjusted odds of blood-culture ordering in $POCT^+$ patients divided by an adjusted odds of blood culture in $POCT^-$ patients with similar calculations for $ST^+$ or $ST^-$ groups and for CBC, UA, UCx, antibiotics-used or inpatient admission with the resulting ratios listed below in Table 2.<br>• No differences were noted with positive Influenza test results on antibiotic used, admission rates, ED expenses or length of stays. |

| | | |
|---|---|---|
| | | • No positive blood or urine cultures were obtained in any Influenza positive patient in either POCT or ST groups. |
| **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?** | Possibly, if staff can receive similar training to identify febrile children and rapidly, appropriately obtain specimens and POCT results. |
| **B.** | **Are the results applicable to the patients in my practice?** | Yes, SLCH patients likely similar to University of Cincinnati pediatric population. |
| **C.** | **Will the results change my management strategy?** | Yes, if recognition among parents and PCP's that moderately sensitive, highly specific POCT like QuickVue convey extremely low risk of SBI in test-positive subjects who present to ED for evaluation of fever during regional influenza outbreaks, these tests could prevent the ordering of unnecessary tests like UA and urine cultures (and possibly blood cultures). |
| **D.** | **Will patients be better off as a result of the test?** | Yes, if unnecessary tests are not ordered |
| | | |

**Limitations:**

1) **Industry-sponsored trial with the potential for bias, although sponsors reportedly had no access to data or manuscript and results don't entirely support use of their product.**
2) **Under-powered to detect significant difference if one truly exists.**
3) **Possible *ascertainment bias* on true rate of bacteremia or UTI since not all subjects had blood culture or urine culture.**
4) **Pseudo-randomized design may have under-represented certain clinicians and their respective practice patterns, but the authors expressed valid ethical concerns for their study design based upon the limitations of their physical environment.**
5) **Lack of external validity without similar training of ancillary staff obtaining specimens for rapid-testing.**
6) **Relied on parental recall for immunization status.**
7) **Results only applicable to time-periods of Influenza outbreaks.**

**Bottom Line:** **When compared with batch-testing (which is not readily available while evaluating patients in the ED), positive POCT for Influenza in children ≤ 3 yrs old presenting to one ED with fevers ≥ 38° (2-3months old) or ≥ 39° (3 months to 3 years old) reduced ordering UA or urine cultures and may reduce blood culture and CBC-ordering in appropriately powered studies. While awaiting such trials, selective application of POCT for Influenza may be helpful for physicians considering additional ancillary testing of blood or urine. A positive Influenza test is associated with a very low (zero) rate of bacteremia or UTI in the current study.**

**Table 1**
**Clinician Test Ordering Stratified by Influenza Test Result**

| Test/Treatment Ordered in ED | POCT | | ST | | P-value |
|---|---|---|---|---|---|
| | + | - | + | - | |
| Blood culture | 13.3% | 28.8% | 24% | 29.4% | 0.006 |
| Antibiotics | 6.7% | 19.6% | 9% | 19.6% | < 0.001 |
| CBC | 13.3% | 30.8% | 25% | 31% | 0.002 |
| UA | 7.6% | 26.7% | 20% | 21.2% | < 0.001 |
| Urine culture | 7.6% | 25.8% | 20% | 21.2% | < 0.001 |
| LP | 0 | 2.9% | 3% | 0.8% | 0.09 |

**Table 2**
**Clinician Test Ordering Stratified by Influenza Test Result**
**Adjusted Odds of Ordering Test if POCT is Positive**

| Test/Treatment Ordered in ED | POCT | ST | P-value |
|---|---|---|---|
| Blood culture | **0.59** | **0.71** | **0.088** |
| CBC | **0.56** | **0.69** | **0.058** |
| UA | **0.45** | **0.67** | **0.002*** |
| Urine culture | **0.46** | **0.67** | **0.005*** |
| Antibiotics | **0.53** | **0.57** | **0.703** |