Critical Review Form

Diagnostic Test

Accuracy & Impact of a Point-of-Care Rapid Influenza Test in Young Children with Respiratory Illness, *Arch Pediatr Adolesc* Med 2006: 160:713-718

Objectives: **To evaluate "the impact of using a rapid test for influenza among outpatient children with fever or acute respiratory symptoms" using viral culture and polymerase chain reaction assays to independently define Influenza positive or negative cases in testing the hypothesis "that such tests would impact patient care by reducing unnecessary diagnostic testing, decreasing antibiotic use, and increasing antiviral use". (p.713)**

Methods: **Convenience sampling of immunocompetent children under age 5 presenting to Vanderbilt University Medical Center's pediatric ED or acute care clinic with cough, rhinorrhea, wheezing, difficulty breathing, fever, sore throat, apnea, or ear pain during Tennessee health department defined influenza seasons in 2002-2003 and 2003-2004. Exclusion criteria included prior enrollment or chemotherapy-related febrile neutropenia. Children were enrolled 3-days per week in the ED and 1-day per week in the acute care clinic. Study days were randomized to rapid test or no rapid test days using blocks of 4 and 6 using a STATA random number generator.**

The POCT was QuickVue Influenza Test (Quidel Corp, San Diego, CA) and the Gold Standard was viral culture immunofluorescence assay at 10-days and colorimetric microtiter plate system reverse transcription polymerase chain reaction (rt-PCR). A specimen was considered Influenza-positive if *either* the viral culture or rt-PCR was positive for Influenza A or B. Specimens were collected by a study nurse who received formal training using the QuickVue Kit and American College of Pathologist laboratory proficiency tests 3-times each year.

The primary outcome "was the proportion with any diagnostic tests, except a rapid influenza test ordered by the treating physician and no performance of the rapid tests groups" (p.714). Secondary outcomes looked at individual diagnostic tests: CBC, urinalysis, blood or urine cultures, and/or chest x-ray, as well as antibiotic or antiviral prescriptions. Differences between groups were analyzed statistically with Chi-squared or Fisher exact tests and a Kappa analysis of interrater reliability was performed on 102 randomly selected test strips for the QuickVue. The

study had 80% power with α 0.05 to detect 15% testing difference with 185 children each in rapid test and no rapid test group, although post-hoc analysis was performed when different testing noted between ED and the acute care clinic showing the clinic portion of the study was underpowered to detect a difference based on observed testing rates.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did clinicians face diagnostic uncertainty?**	Yes – febrile children < 5 yrs old with fever and acute respiratory symptom.
B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group? (Confirmation Bias)**	Yes – Gold standard rt-PCR or viral cultures "were performed by research laboratory personnel blinded to the results of the rapid influenza tests" (p.714)
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard? (Ascertainment Bias)**	No – all subjects had gold standard viral cultures and rt-PCR testing performed.
II.	**What are the results?**	

A.	**What likelihood ratios were associated with the range of possible test results?**	• 92% of eligible children were approached in the ED for consent during enrollment times (84% were in the acute care clinic). No significant differences existed between children enrolled or rapid-test vs. no rapid test days (Table 1, p 715) although children in the ED were significantly younger than those in the clinic. • Children with influenza had a mean symptom duration of 3.9 days although 24% of Gold Standard proven influenza met criteria for antiviral therapy. • None of the children in the clinic were admitted, while 13% of those in the ED were admitted (p <0.001) • The mean number of diagnostic tests per child was significantly higher in the ED than the clinic (1.1 vs. 0.2, p <0.001). In terms of total numbers in the ED 141 diagnostic tests were ordered on 305 subjects compared with the clinic 24 diagnostic tests on 163 subjects. **QuickVue test characteristics 2x2 table** Sensitivity = 82% (95% CI 69-92) Specificity = 99% (95% CI 96-99) Prevalence = 25% LR + = 126 (95% CI 18-898) LR - = 0.18 (95% CI 0.10-0.32) Kappa = 0.98 • Fewer ED children in the rapid-test group (regardless of the rapid test result) had further diagnostic tests ordered (39% vs. 52%, p=0.03 Table 2 p.716). However, in the ED there was a trend towards less CXR in QuickVue + subjects (11% vs. 24% ordered, p=0.18). No such trend was noted in the clinic. • Rapid testing did not impact ordering CBC, UA, cultures, antibiotics, or antivirals in ED or clinic.

	VCx or rt PCR +	VCx or rt PCR -
QuickVue +	42	1
-	9	153

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?**	Yes – with proper training and skill maintenance from those who will be collecting specimens and interpreting QuickVue results.
B.	**Are the results applicable to the patients in my practice?**	Yes. Nashville children (under age 5) and Pediatric EM clinicians undoubtedly are similar to St. Louis children.
C.	**Will the results change my management strategy?**	Yes, although the impact of POCT likely will "vary by influenza season and between the beginning and end of each season" (p.717). The current trial offers single center confirmation of the diagnostic performance of QuickVue Influenza POC testing by trained nurses in the ED setting in children under age 5. Appropriate use of this test may offer timely regional influenza surveillance data not currently available with viral cultures or rt-PCR to impact public health decision like school closure and close-contact prophylaxis. The observation that 24% of influenza positive children met criteria for antiviral therapy which only 1 child received is disturbing. Furthermore 20% of children with influenza had antibiotics prescribed. Did these children have secondary bacterial infections or is this further evidence of a gap between knowledge and best practice EM.
D.	**Will patients be better off as a result of the test?**	Yes, if antiviral therapy can be initiated, appropriate vaccinations emphasized and close contacts prophalaxed, while avoiding unnecessary diagnostic testing and antibiotic prescribing.

Limitations:

1) **Single center convenience sampling with potential limited external validity and under/over representation of particular clinicians practice patterns.**
2) **Results only applicable during routine influenza season. Results should not be extrapolated to non-flu season or during influenza epidemic.**
3) **No analysis of presence of secondary bacterial infections prompting antibiotic use (pneumonia, otitis media).**
4) **No testing of other affects of rapid testing like alleviation of parental anxiety or ED length-of-stay.**

Bottom Line:

QuickVue Influenza test is a useful POC test in children under age 5 with LR+ 126 and LR- 0.18 with excellent reproducibility (Kappa = 0.98) when obtained by trained research nurses in those with non-specific upper respiratory symptoms. Despite these admirable test characteristics at Vanderbilt Medical Center, a positive QuickVue test does not appear to impact overall or test-specific diagnostic testing, antibiotic prescribing or appropriate antiviral use. Appropriate use of POC tests like QuickVue have the potential to reduce ED LOS and inappropriate testing/prescribing while relieving parental anxiety and maintaining up-to-date regional surveillance data, but further studies will be needed to assess the utility and acceptability of these possibilities at various health care settings.