Outcomes with Multiplex PCR Respiratory Sample Testing on Hospital Inpatients

Outcomes and Cost Associated with a Multiplex PCR System on Nasopharyngeal Swab Specimens (FilmArray Respiratory Panel) in a Large Tertiary Inpatient Hospital Population

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Abstract: While respiratory Multiplex PCR (FilmArray) testing provides reliable diagnostic data, its cost-effectiveness in the management of influenza within our health system is unclear. We conducted a retrospective cohort study to evaluate FilmArray results and associated management in 456 adult hospital patients. Results indicate that influenza was rare within our cohort and that antibacterials were infrequently de-escalated following positive influenza results, which highlights the need for additional education regarding appropriate use of the FilmArray test and its results.

Background: Respiratory infections caused by viral and bacterial pathogens are the second most common cause of morbidity and mortality worldwide. (1) Without a definitive diagnosis, patients with viral infections are more likely to receive unnecessary antibiotic therapy. (2) A number of rapid testing modalities are available with varying sensitivities to detect respiratory viruses. The FilmArray Respiratory Panel (RP) (BioFire) ™ Diagnostics, Inc., Salt Lake City, UT, USA is the first multiplex PCR molecular panel cleared by the US FDA for the detection of both bacterial and viral respiratory pathogens. Sensitivity and specificity have been reported to range from 80-100% and 100%, respectively. The FilmArray targets 20 pathogens, including 17 viruses and 3 bacteria. (3). The FilmArray panel allows for increased detection of respiratory viral pathogens, enabling health care providers to determine the need for ancillary testing, antibacterial, or antiviral therapy and motivate decision regarding hospitalization and infection
control measures. Estimating cost-effectiveness is vital to understanding and promoting appropriate use criteria for a given test. The FilmArray is a relatively expensive test compared to the older, less sensitive test for influenza A virus (rapid nasal swab testing). The sensitivity for the latter is so low that the CDC recommends starting anti-influenza treatment empirically if symptoms warrant and not to rely on the testing modality.

**Methods:** Our primary goal was to investigate the direct costs of using respiratory FilmArray in our health system. We conducted an audit of clinical laboratory records, which retrieved all patients who had received the respiratory FilmArray test over a two-year span. Further analysis allowed us to select only hospital inpatients over age 18 which became our sample. A retrospective cohort study was then conducted based on this sample. The study period was from March 1, 2013 through March 1, 2015. Study approval was granted by the Institutional Review Board, and informed consent was not obtained. Collected patient information included: age, gender, FilmArray result, hospital length of stay, whether anti-influenza therapy was prescribed, if antibacterials were prescribed, if antibiotic de-escalation occurred based on the results of the FilmArray (e.g. discontinuing antibacterials if the FilmArray result was positive for influenza), and patient disposition after the index hospital stay. Additionally, since secondary *Staphylococcus aureus* respiratory tract infections are associated with influenza, we assessed the incidence of these infections in our cohort. Our definition was a listed discharge diagnosis of upper respiratory infection or pneumonia with this pathogen present in respiratory cultures. Finally, we assessed costs of FilmArray testing in this cohort based on our laboratory costs of $210 per test. This includes reagents/testing supplies plus labor as estimated from our Laboratory department. Descriptive statistics were calculated for patients. Variables were presented with counts and percentages.

**Results:** Our cohort consisted of 456 hospital inpatients who were tested for influenza via respiratory FilmArray during the two years examined. The mean age of our cohort was 65.7 years (median 67 years, interquartile range 24 years), and 56% of our patients were female. Overall hospital length of stay was 15.2 days (median 5.9 days, interquartile range 6 days, total range 1-62 days). Of the 456 patients, a positive result for influenza A or B occurred in 46 patients (10%). Oseltamivir was prescribed in 42 of 46 cases who were positive for influenza and in 8 cases empirically before FilmArray results returned negative (mean dose received in these 8 patients was 1 dose). Systemic antibiotics were prescribed empirically or definitively in 382 patients (84%) of our cohort. These patients had upper respiratory infection or pneumonia as a listed discharge diagnosis (primary or secondary) in all cases. Patients with positive influenza FilmArray results had other antibacterials de-escalated within 48 hours in 8 patients (17%) of cases.

Fifteen *Staphylococcus aureus* respiratory tract infections were documented in our study population. Two were in patients with a positive influenza FilmArray test (4.3%) and 13 in those with a negative test (3.2%). Eight of these patients had Methicillin-Resistant *S. aureus* cultured. Using a base cost of $210 per FilmArray test, the total cost of testing in our cohort was $95,760, or $2,081 per positive test.

**Discussion:** The incidence of a positive influenza A or B result from the respiratory FilmArray
in this cohort was rare. This finding exposes the high cost ($2,081) per positive test that was spent by our institution over the course of 2 years. In addition to this large expense, antibacterials were de-escalated in only 17% of patients with a positive influenza FilmArray test.

These results differ from other previously published studies. Nelson and colleagues published an economic analysis of the respiratory FilmArray test in children (5). These authors based their projections and analysis on an 2003 report that found an older rapid screening test (not the FilmArray assay) had a 24.5% positive result for influenza. Their conclusions were that while the respiratory FilmArray test is quite expensive, its effectiveness in detecting influenza makes it “within the threshold for adopting new cost-effective technologies.” Additionally, Rogers and colleagues evaluated the impact of the respiratory FilmArray test on patient outcomes at the Children’s Healthcare of Atlanta.7 They evaluated patient outcomes in patients tested with a limited PCR panel to patient outcomes in those tested with the multiplex respiratory FilmArray test. Influenza A or B was positive in 92/771 FilmArray patients (15.3%). Patients tested with the respiratory FilmArray had a statistically significant shorter duration of antibiotic use (p=0.003), potentially leading to an estimated decrease in antibiotic and hospital costs. It is worth noting that the studies discussed were conducted primarily in children and little data on the costs associated with the FilmArray test in adults has been published to date.

One of the potential weaknesses of our study is that we collected data for all months in our 2 year study period, differing from the study conducted by Nelson and colleagues, where data collected only during peak influenza season demonstrated statistically significant shorter duration of antibiotic use with the FilmArray test (5). Nonetheless the low yield for influenza relative to the cost of this test suggests that pre-test probabilities should be assessed before FilmArray is used by the providers in our health system. This is an area of education that our health system will address in the future. Additionally the retrospective nature of the study did not allow us to capture information such as initial presenting symptoms or when the FilmArray test was conducted relative to admission.

**Conclusion:** Respiratory FilmArray test results within our study cohort reveal a low number of confirmed influenza A and B, potentially indicating inappropriate use of this test within our institution. Additionally, antibacterial use was not de-escalated in the majority of positive influenza cases. In order to decrease costs and increase patient outcomes, providers can be better educated on appropriate use of the respiratory FilmArray and its results.

**References:**


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