# C-368 IMPLEMENTATION OF NON-BATCHED RESPIRATORY VIRUS ASSAY SIGNIFICANTLY IMPACTS PATIENT OUTCOMES IN THE ICU

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## ABSTRACT- revised

**Background:** Nucleic acid amplification and detection of respiratory virus (RV) pathogens is rapid and sensitive, but multiplex methods can be costly. Implementation of molecular methods promotes improvement in turnaround time (TAT) and increased laboratory workflow efficiency; however, few studies assess the impact of rapid results on downstream patient outcomes. The purpose of this study was to assess the impact of rapid multiplex RV testing for an ICU patient population.

**Methods:** Geisinger Medical Center (GMC) is a 560 bed quaternary care hospital within an integrated health service organization of 8 hospitals, which serves >2.6 million residents throughout 45 counties in Pennsylvania. The GMC standard is to perform multiplex RV testing for all admissions with respiratory symptoms. Between Nov 1, 2010 and Mar 19, 2012, batch molecular RV testing (pre-intervention) was performed once per day. Between Mar 19, 2012 and Apr 30, 2014, RV testing (BioFire Diagnostics) was performed on a first-in first-out (FIFO), random access basis (post-intervention) with priority to ICU and ED locations. A quasi-experimental study design was used to compare retrospective categorical and continuous data from pre- and post-intervention cohorts. The following data variables were analyzed using descriptive and comparative statistics in JMP ver. 12.0.1: collect to report time (CTR), 28 day mortality, length of stay (LOS), ICU days, ventilator days, anti-microbial (including viral and bacterial) utilization, laboratory test utilization, and total cost.

**Results:** Pre- (n=276) and post-intervention (n=460) cohorts showed similar data distributions for age, gender, diagnosis-related group, percent positive results, and treatable viruses detected. The following data variables showed statistical post-intervention improvement (by chi-squared analysis): 28 day survival, LOS, ICU days, ventilator days, anti-microbial utilization, laboratory test utilization, and total cost. The mean CTR was reduced by 30.4 hrs for the post-intervention period and was associated with significantly improved mortality when results were reported in < 7 hr. Patients with positive RV results (any positive result) displayed a significant reduction in mortality (P < 0.05). A 50% decrease in mortality was also observed for Flu A-positive patients; however, due to sample size the difference was not statistically significant. For patients with negative RV results, mean ICU stay, mean overall LOS, and mean total cost decreased by 3.3 days, 1.9 days, and $8,104, respectively.

**Discussion:** Rapid molecular results can improve downstream patient and operational outcomes. Although random access molecular methods tend to be more costly than batch molecular assays, improved outcomes in certain populations, such as ICU, may warrant their use. A plan for action, driven by the test result, and attention to monitoring and improving CTR as a quality indicator appears to be an important strategy. Additionally, this study demonstrated that 28 day mortality increased when results were reported in > 7 hours. Although a FIFO workflow may not be feasible for some laboratories, it may be possible to implement batch testing to achieve similar CTR. Lastly, the increased sensitivity and rapid result can promote antimicrobial stewardship and minimize overall healthcare costs per visit. Population-specific analysis is warranted for different medical practices and patient populations.

## METHODS

**Experimental Aim:** To assess the impact of rapid diagnostic testing for RV pathogens on downstream healthcare metrics, such as length of stay, resource utilization, and antimicrobial stewardship.

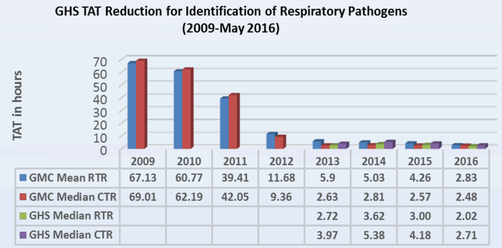
**Study Design:** This is a retrospective, observational study, which assessed the impact of RV testing during the 2010-2014 RV seasons. The data extraction included data from subjects at Geisinger Medical Center. The cohort was assembled by extracting data from the laboratory information system (LIS) and the electronic health record (EHR). This study follows the protocol outlined in the approved IRB # 2015-0103.

**Sample Size:** Pre-intervention n = 276, Post-intervention n = 460.

**Dates:** Nov 1, 2010 - Apr 30, 2014.

**Software:** LIS software (Sunquest) was used to extract all respiratory panel results to drive clinical data extraction from EPIC v. 2014. JMP ver. 12 and Excel 2013 were used for data validation, statistical analysis, and specialty graphs (Figures 1-6).

**Laboratory Method Intervention:** FilmArray Respiratory Pathogen Panel (BioFire Diagnostics)




| | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 |
|---|---|---|---|---|---|---|---|---|
| GMC Mean RTR | 67.13 | 60.77 | 39.41 | 11.68 | 5.9 | 5.03 | 4.26 | 2.83 |
| GMC Median CTR | 69.01 | 62.19 | 42.05 | 9.36 | 2.63 | 2.81 | 2.57 | 2.48 |
| GHS Median RTR | | | | | 2.72 | 3.62 | 3.00 | 2.02 |
| GHS Median CTR | | | | | 3.97 | 5.38 | 4.18 | 2.71 |

**Figure 1. Recent Timeline of Respiratory Pathogen Testing for Molecular Multiplex RV Methods by Calendar Year.** Geisinger Medical Center (GMC) and Geisinger Health System (GHS) depicts system-wide attention to continuous reduction in Receipt Time to Result (RTR) and Collect Time to Result (CTR).

## DEMOGRAPHICS

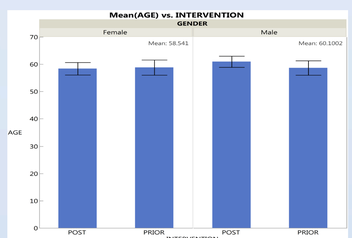



**Figure 2. Distribution of Age and Gender by Intervention.** No statistical difference between age or gender distribution exists among pre- or post-intervention groups. Mean overall female age was 58.5 yr; mean male age was 60.1 yr.

## RESULTS

### DATA DISTRIBUTIONS

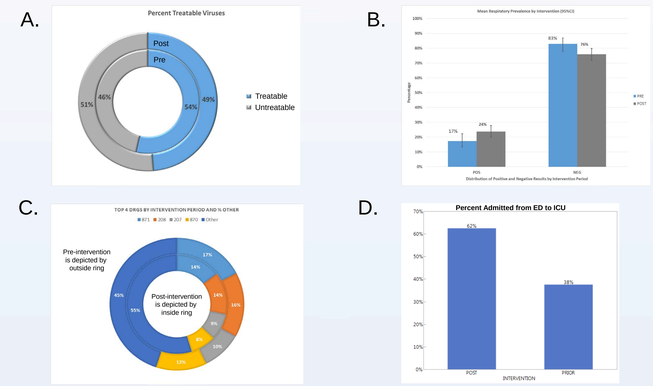



**Figure 3. Distribution of Data Variables Depicts Similarity of Intervention Groups.** A) Proportion of treatable viruses by intervention, no significant difference (NSD) ; B) Proportion of test results by intervention (of total positives shown, 32% were Flu A: H3 in post-intervention group vs. 50% Flu A: H3 in pre-intervention group), NSD. Error bars represent CI; C) Diagnosis-related group (DRG) distribution, NSD overall, top 5 depicted (207: Respiratory System Diagnosis with Ventilator Support 96+ Hours , 208: Respiratory System Diagnosis with Ventilator Support < 96 Hours, 870: Septicemia or Sever Sepsis with Mechanical Ventilation 96+ Hours, 871: Septicemia or Severe Sepsis without Mechanical Ventilation 96+ Hours); D) Percent with illness requiring hospital admission from the ED to the ICU by intervention, post-intervention group has higher incidence of admission than pre-intervention group, suggesting equal or more severe ED cohorts; severity score analysis pending.

### CLINICAL AND OPERATIONAL OUTCOME DATA

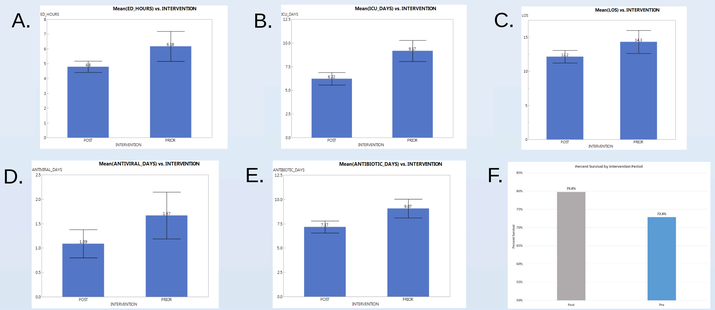
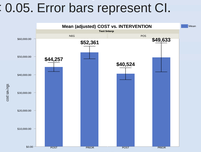



**Figure 4. Outcome Data**. A) Time in Emergency Department (ED) Hours reduced by 1.4 hr, P < 0.02; B), Intensive Care Unit (ICU) days decreased by 3.0 days, P < 0.0001; C) Total Length of Stay (LOS) reduced by 2.1 days, P < 0.03; D) Antiviral Days decreased by 0.58 days, P < 0.05 (NSD by $CI_{95}$ but is significantly different by Wilcox-Rank Sum analysis); E) Antibiotic Days decreased by 1.9 days, P < 0.002; F) Relative survival increased by 10%, P < 0.02. Data not shown but statistically improved for: total test utilization, and ventilator days, P < 0.05. Error bars represent CI.

**Figure 5. Savings in Total Costs by Result**. When compared to costs from the batch RV test (pre-intervention) period, rapid reporting of negative results saved an avg. of $8,104/visit and positive results saved and avg. of $9,109/visit in the post-intervention period. Error bars represent SEM.



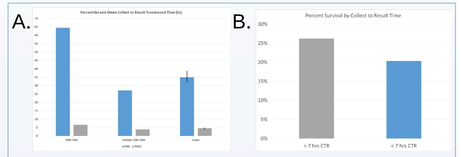




**Figure 6. Collect to result (CTR) time.** A) The 90th percentile of mean was reduced 89.8% in post-intervention. The 50th percentile was reduced 86.0% in post-intervention. Mean CTR decreased by 30.4 hrs (87%). Error bar represents CI; B) When combined CTR time was substratified, the percent survival at 28 d significantly increased for persons in the GMC ICU cohort when results were delivered in ≤ 7 hrs (P < 0.04).

## CONCLUSIONS

- The FilmArray is a random access instrument which eliminates the need for batch testing and may significantly reduce CTR time in a variety of healthcare settings
- At GMC, CTR times greater than 7 hours can increase 28 day mortality in an ICU setting. Further confirmation in other healthcare settings is warranted.
- Impact to patient outcomes were observed in GMC ICU via significant reductions (P < 0.05) in:
  - ED wait times per pre-admission visit
  - ICU days per ICU visit
  - LOS per ICU visit
  - Antibiotic days per visit
  - Ventilator days per visit
  - 28 day all cause mortality
  - Total number laboratory orders
  - Total cost per visit
- **Limitations**
  - Viruses detected are not equal between the pre- and post-intervention groups; more were detected in post-intervention
  - DRG severity of illness should be fully assessed.
  - Although practical, a quasi-experimental study design has limitations.

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