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Near point-of-care adoption of Cepheid Xpert® Flu/RSV XC testing within an integrated healthcare delivery network

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ABSTRACT

Flu/RSV testing was implemented in out-patient clinic-based physician office laboratories throughout Pennsylvania. On-site testing reduced the collect-to-result time by 70% when compared to testing in a centralized core laboratory; over- or under-treatment for influenza A and B (measured by anti-viral prescription) was reduced by 15% ($P < 0.0001$). Antimicrobial prescription was not affected by on-site testing.

Due to its unpredictable nature, respiratory virus season challenges healthcare organizations world-wide. Emergency departments experience a sharp increase in patients presenting with influenza-like-illnesses (ILI) (Ko and Drews, 2017). Bed management, workforce shortages, antiviral shortages, and antimicrobial stewardship strategies are especially challenging during the respiratory virus season. Recent development and implementation of accurate and rapid CLIA-waived nucleic acid tests for Flu/RSV detection supports frontline healthcare providers with actionable results (FDA, 2018; Vashist et al., 2015), which can help mitigate the challenges of the season and help support pandemic preparedness. To that end, as a large integrated health care system laboratory, we designed the FluWorks program, which was launched during the 2016–2017 flu season. Before launching CLIA-waived testing, we implemented Flu/RSV testing, using the Cepheid Xpert® Flu/RSV XC (CLIA- moderately complexity) in 8 Geisinger Rapid Response Laboratories (RRLs) throughout central and northeastern Pennsylvania to assess impact, speed, accuracy, and workflow processes.

Before implementation, clinic laboratory infrastructure was redesigned to include training of personnel in molecular practices, assessment of operations and staffing, method verification at multiple locations, and limitations in clinic space (Arboleda and Garner, 2017). The challenges of limited dedicated space, space not originally engineered for molecular testing, large footprints of molecular dead-air boxes, and molecular training requirements presented challenges, which were mitigated by custom design and crafting of dead-air boxes to contain sample preparation and cartridge loading. Doctoral staff and analytical specialists from Geisinger's core laboratory trained the RRL personnel with a 4 h online course describing the basics of molecular testing, decontamination procedures, and amplicon control. RRL medical laboratory staff were then trained on site to use the Xpert® cartridges by core laboratory staff and by the vendor. Method verification for both Xpert® Flu/RSV XC (moderate complexity) and Xpert® Xpress Flu/RSV tests (waived testing) was performed using Zeptometrix controls (NATtrol Influenza/RSV Verification Panel, Buffalo, NY), and tested for 20 days. Precision was documented to be 98% across all sites. Competency samples (samples with known results from Biofire FilmArray Respiratory Panel, Salt Lake City, UT) were tested by all operators (2 operators per site, 16 total) who were blinded to original results. 100% concordance for competency samples was observed.

On-site patient testing with Xpert® Flu/RSV XC test occurred from November 1st, 2016 to January 19th, 2017 (on-site cohort, n = 362). Outcomes were compared to those from patients collected in the clinic laboratory but transported to the central laboratory for testing from February 25th to April 25th, 2017 (courier cohort, n = 189). The courier cohort time period was selected to provide matched proportions

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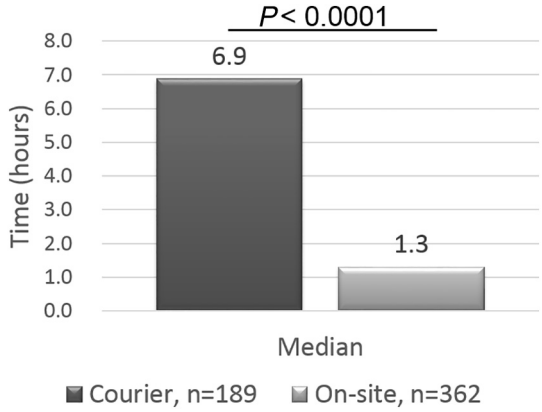

Fig. 1. Collect-to-result time comparison between Flu/RSV testing at near point-of-care locations vs samples transported by courier to a central laboratory.

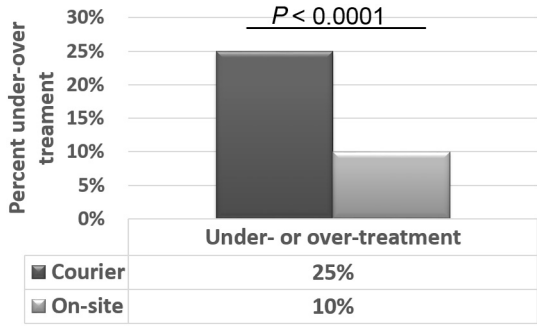

Fig. 2. Antiviral prescription comparison between Flu/RSV testing at near point-of-care locations vs samples transported by courier to a central laboratory.

between cohorts for virus prevalence (influenza A/B and RSV), age, and gender. Selection of cohorts within the same winter ensured similarity in intrinsic provider behavior so impact of on-site testing could be measured.

Between cohorts the same proportion of males to females was observed, nearing 50% for each [184 females in on-site cohort (50.8%) and 103 in courier cohort (51.4%)]. When substratified by age, no significant differences were noted between cohorts; however, the overall sample distribution was skewed towards ages <5 y [157 children <5 y of age in on-site cohort (43.3%), 61 in courier cohort (32.3%)]. The percent positivity for FluA/B samples was 16.9% for samples tested on site compared with 16.4% for samples transported by courier. During on-site testing, the collect-to-result time (CTR) was reduced by 70% using the Xpert® Flu/RSV XC cartridge, which provides results in ≤1 h ($P < 0.0001$) with median CTR of 6.9 h for courier to 1.3 h for on-site (Fig. 1). The overall range CTR, among the RRL sites, was 3.77–10.29 h (3.30–10.94 h 95% CI) for the courier group, and 1.79–2.24 h (0.63–3.85 h 95% CI) for the on-site cohort. No significant differences in CTR range were noted between any of the RRL sites for either of the 2 testing periods. In terms of antiviral stewardship during the courier period, 25% of subjects did not receive optimal therapy (e.g. receiving Oseltamivir when the Flu tests were negative, or not receiving Oseltamivir when the test was positive for FluA or B). When testing occurred on site, the proportion of under- or over- treated dropped to 10% ($P < 0.0001$, Fig. 2). In contrast, antimicrobial prescription, was not affected by the faster CTR in the presence or absence of viral infection. This finding aligns with work published by others (Green et al., 2016; Ko and Drews, 2017). During the 2016–2017 flu season, we calculate that for every USD invested in reagents and technologist time, the recovered costs from antiviral therapy, which did not need to be prescribed for RSV or for negative samples, was $6.3 USD for every dollar invested. If capitol acquisition was included, the return was $1.1 USD for every dollar spent.

Using the moderate complexity method (TAT = 60 min) the FluWorks program was associated with a significant reduction in CTR and antiviral prescriptions. An opportunity for antibacterial stewardship for future flu seasons still remains. The 2016 launch of FluWorks established standard of care testing for the Geisinger community and better prepared our laboratory system to distribute workload and improve preparedness for future pandemics. Documented antiviral stewardship of FluWorks testing supports precision therapy for our population and preservation of antiviral medication in routine and pandemic situations. Implementation of nucleic acid tests in out-patient settings contributed to improved operational outcomes and antiviral stewardship and supports the concepts of precision medicine and population health. Given the matched cohorts, the results achieved with the FluWorks intervention should be generalizable to other integrated healthcare delivery networks with stewardship programs in place and may be generalizable to point of care settings.

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