150. the RAPID trial: randomized Controlled Trial assessing point-of-care influenza and Other Respiratory Virus diagnostics in the Pediatric ED Setting

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Session: O-29. Innovations in Diagnostics

Background: Respiratory illnesses represent one of the commonest reasons for pediatric visits to the ED, and over 50% of these children are prescribed antibiotics despite a viral etiology in most cases. Our objectives were to determine whether rapid respiratory pathogen (RRP) testing decreases antibiotic and health care utilization among children evaluated in the ED with a respiratory illness.

Methods: We conducted a randomized controlled trial among children 1 mo-18 yrs of age attending an ED with influenza like illness (ILI). All children received a nasopharyngeal swab for RRP testing, and were randomized to the *intervention group* (result given to providers and parents) or *control group* (result not given, routine clinical care). Families were interviewed on enrollment, 1 and 10 days later. The *primary outcome* was antibiotic use. *Secondary outcomes* included antiviral use, hospitalization and recurrent medical visits. Intention to treat (ITT) (assigned group) and pragmatic (provider knows test results) analyses were conducted using SAS v 9.4. Pragmatic analyses were adjusted using multivariable Poisson regression.

Results: Among 920 visits (890 children) with ILI, 795 (85%) were RRP positive. Sociodemographic characteristics between groups were similar; 37% of children in the intervention group were discharged before results were available and 12% of children in the control group underwent clinical testing. The median age was 2.1 yrs (IQR 0.88–5.6); 35% had high-risk comorbidities. In the ITT intervention group, children were more likely to receive antibiotics (RR 1.3, 95% CI 1.0–1.7) (Table 1). In adjusted pragmatic analyses, children with known results were more likely to receive antivirals (RR 2.6 95% CI 1.5–4.3) and be hospitalized (RR 2.0, 95% CI 1.5–2.7); antibiotic use was not significant (Table 2). Children testing negative for a virus were more likely to receive antibiotics than those with a virus (35% vs 23%, p = 0.01).

Table 1. Clinical Outcomes by Study Arm, Intention to Treat Analyses

Clinical Outcomes of interest- Intention to treat analyses					
Outcomes of Interest	Total (n=908)	Intervention (n=452)	Control (n=456)	Risk Ratio or Geometric Ratio (95%CI)	P-value
Antibiotics prescribed/received	203 (22)	115 (25)	88 (19)	1.3 (1.0,1.7)	0.03
Antivirals prescribed/received	56 (6)	31 (7)	25 (5)	1.3 (0.8,2.1)	0.39
Antivirals prescribed/received and Influenza positive	48 (5)	25 (6)	23 (5)	1.1 (0.6,1.9)	0.74
ED Length of stay, hours (geometric mean, 95% CI)	3.1 (3.0,3.2)	3.1 (2.9,3.3)	2.8 (2.0,4.5)	1.03[a] (0.95,1.12)	0.44
Hospitalized from ED	146 (16)	77 (17)	69 (15)	1.1 (0.8,1.5)	0.44
Additional Hospitalizations within 10 days (chart review)	27 (3)	15 (3)	12 (3)	1.3 (0.6,2.7)	0.54
Additional ED visits within 10 days (chart review)	58 (6)	29 (6)	29 (6)	1.0 (0.6,1.7)	0.97
Additional medical visits (parental report, n=620)	161 (26)	85 (27)	76 (25)	1.1 (0.8,1.4)	0.53

a- geometric ratio

Table 2. Clinical Outcomes by Study Arm, Pragmatic Analyses

Clinical Outcomes of interest -Pragmatic analyses (unadjusted, adjusted)						
Outcomes of Interest	Total (n=907)	Provider knows results (n=340)	Provider does not know results (n=567)	Unadjusted Risk Ratio or Geometric Ratio (95%CI)	Adjusted[a] Risk Ratio or Geometric Ratio (95%CI)	P-value (adjusted)
Antibiotics prescribed/received	203 (22)	90 (26)	113 (20)	1.3 (1.0,1.7)	1.09 (0.92,1.30)	0.31
Antivirals prescribed/received	56 (6)	34 (10)	22 (4)	2.6 (1.5,4.3)	2.52 (1.50,4.23)	0.0005
Antivirals prescribed/received and Influenza positive	48 (5)	29 (9)	19 (3)	2.5 (1.5,4.5)	2.5 (1.41,4.34)	0.0016
ED Length of stay, hrs (geometric mean, 95% CI)	3.1 (3.0,3.2)	4.1 (3.9,4.4)	2.6 (2.5,2.7)	1.60[b] (1.48,1.74)	1.9[b] (1.69,2.05)	<.0001
Hospitalized from ED	146 (16)	83 (24)	63 (11)	2.2 (1.6,2.9)	2.0 (1.50,2.72)	<.0001
Additional Hospitalizations within 10 days (chart review)	27 (3)	15 (4)	12 (2)	2.1 (1.0,4.4)	2.0 (0.97,4.19)	0.06
Additional ED visits within 10 days (chart review)	58 (6)	20 (6)	38 (7)	0.9 (0.5,1.5)	0.9 (0.55,1.56)	0.78
Additional medical visits (parental report)	161 (26)	65 (28)	96 (25)	1.1 (0.9,1.5)	1.1 (0.87,1.49)	0.34

a-adjusted for high-risk condition, age and diagnosis
b-geometric ratio

Conclusion: Knowledge of testing led to a paradoxical increase in antibiotic prescribing, as well as an increase in appropriate antiviral prescribing, ED length of stay and hospitalization. Further studies are needed to assess whether RRP testing with faster turn around times or coupled with stewardship interventions may impact outcomes.

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151. The Use of Dried Blood Spot Cards to Assess Serologic Responses of Individuals Vaccinated Against Measles, Hepatitis A, Tetanus, Influenza and Varicella Zoster

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Background: Traditional blood sampling by venipuncture is cumbersome and expensive. Dried Blood Spot (DBS) sampling is desirable because of its ease of sample collection, transportation and storage. It has been used in clinical diagnosis but not been thoroughly studied for the potential use to assess the immune status of individuals following natural infection or preventive vaccination. The goal of this study is to compare DBS to traditional blood samplings in detection of antibodies in individuals vaccinated against measles, hepatitis A, tetanus, influenza and varicella zoster.

Methods: Blood from 220 vaccinated individuals were collected by venipuncture into serum separation tubes and by fingerstick onto Whatman 903® protein saver cards. ELISA was used to test DBS eluates and serum samples for antibodies against measles, varicella, tetanus and hepatitis A. Sensitivities, specificities, and correlation coefficients were evaluated to compare optical density (OD) values of paired serum and DBS samples. Hemagglutinin inhibition (HAI) and microneutralization assay (MNA) were used to determine anti-influenza antibody in serum and DBS samples. The long term stability of DBS samples at different temperatures was assessed using simulated immune measles blood.

Results: DBS OD was highly correlated with serum OD for antibodies to measles (r = 0.93), varicella (r = 0.82), and tetanus (r = 0.91) (Fig.1). Sensitivities of DBS OD ranged from 86–99% and specificities ranged from 96–100% using cut-offs established by each assay. By contrast, the hepatitis A data showed a low sensitivity (31%) and a weak correlation (r = 0.14) between DBS and serum samples. HAI and MNA assays showed a broad range of anti-influenza A (H1N1 and H3N1) antibody titers in serum samples but failed to detect the antibodies in DBS eluates. The stability data indicated that DBS samples were stable for 4 weeks when stored at room temperature and for 6 months at 4°C (Fig. 2).

Figure 1. Correlation of antibody levels detected by DBS sampling to the antibody levels detected by serum sampling for measles, hepatitis A, tetanus and varicella zoster.

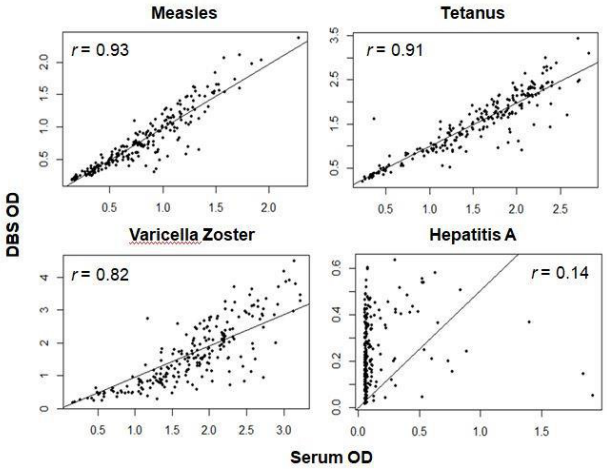
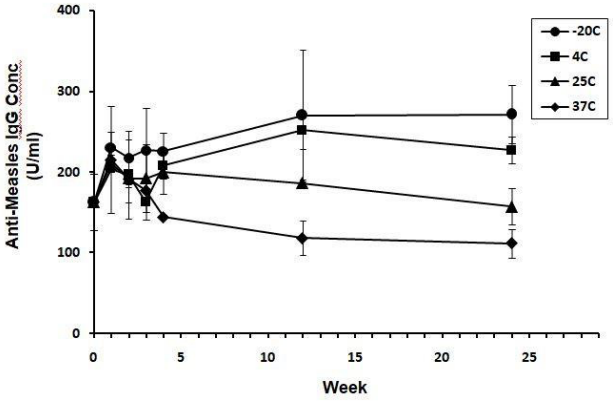


Figure 2. Stability of the blood samples on DBS cards stored under various temperatures for 25 weeks as measured by the titers of anti-measles antibody (IgG) at various time points.



Conclusion: DBS sampling was sensitive, specific, and highly correlated with traditional venipuncture sampling in detection of antibodies against measles, tetanus and varicella zoster, but not hepatitis A and influenza. Thus, the success of using DBS sampling to assess the antibody levels in immunized individuals may be dependent on the pathogens and the type of assay used.

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