Implementation of a Molecular Diagnostic Test for Pediatric Acute Gastroenteritis: The FilmArray GI Panel IMPACT Study

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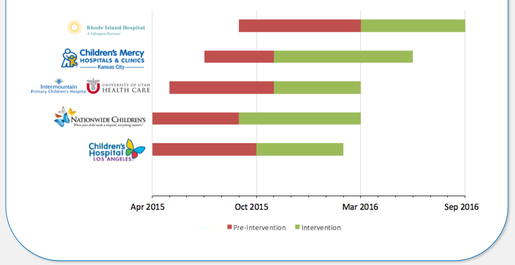
Background

- Diagnosis of the etiology of acute gastroenteritis (GE) with conventional tests is complex, slow and has low yield
- New multiplex molecular tests can identify potential etiology in 50-70% of patients within a few hours
- However, many cases of GE are self-limited and newer tests are expensive
- **Goal of the GI IMPACT study: Measure the impact of multiplex PCR testing in children presenting to Emergency Department with acute GE**

Methods

- Design: Prospective, multicenter, modified step-wedge quasi-experimental study
  - Site initiation based on feasibility, not randomization
- Setting: 5 Academic Pediatric Emergency Departments
- Patients:
  - Children <18 years with acute GE presenting to ED
  - Duration of symptoms >24 hr but <14 days
  - Able to provide stool specimen within 48 hr
- Procedures
  - Structured questionnaire at baseline
  - Chart abstraction
  - Follow up questionnaire at 7-10 days
- Pre-Intervention:
  - After enrollment, physician-directed testing. Stool tested retrospectively by multiplex PCR (FilmArray® GI Panel, BioFire Dx, Salt Lake City)
- Post-Intervention:
  - Providers educated on test platform and pathogens
  - Multiplex PCR on all patients, either in ED or within 2 days
- Outcomes
  - Primary: Additional health care encounters
  - Secondary: Treatable infections, appropriate therapy, time to diagnosis, time to therapy, absence from childcare or work, secondary illness in family
- Analysis as pre- post- study. Unadjusted P values presented

Stepped wedge enrollment



Demographics

	Pre-Intervention period N= 571	Multiplex PCR period N=586	P value
Median Age (IQR)	3 (1.2-7.0)	2.7 (1.2-7.8)	ns
<6 months	53 (9%)	63 (11%)	
6-23 months	163 (29%)	181 (31%)	
2-4 years	153 (27%)	122 (21%)	
5-11 years	132 (23%)	150 (26%)	
12-17 years	67 (12%)	68 (12%)	
Female	300 (53%)	272 (46%)	ns
Insurance			ns
Public	375(66%)	368 (63%)	
Private	147 (26%)	164 (28%)	
None	16 (3%)	22 (4%)	
International travel past month	9 (2%)	14 (3%)	ns
Pet or animal exposure	320 (65%)	331 (65%)	ns
Attend pre-school or daycare (< 5yrs)	85 (32.8%)	72 (28.7%)	ns
Season			<0.001
Summer (Jul-Sep)	310 (54%)	66 (11%)	
Fall (Oct-Dec)	94 (16%)	202 (34%)	
Winter (Jan-Mar)	45 (8%)	214 (37%)	
Spring (Apr-Jun)	122 (21%)	104 (18%)	

Clinical Findings

	Pre-Intervention period N= 571	Multiplex PCR period N=586	P value
Fever	324 (57%)	291 (50)	0.04
Vomiting	450 (79%)	459 (78%)	ns
Diarrhea	473 (83%)	547 (93%)	<0.01
Diarrhea duration before enrollment (days)	2 (1-5)	3 (2-5)	0.08
Bloody diarrhea	52 (11%)	74 (14%)	ns
Stool culture ordered	70	NA	
Shiga Toxin ordered	33	NA	
Viral studies ordered	10	NA	
Antibiotics prescribed	19 (3.3%)	24 (4.1%)	ns
Admitted to Hospital	81 (14%)	96 (16%)	ns

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In memory of Chris Stockmann PhD 1988-2016

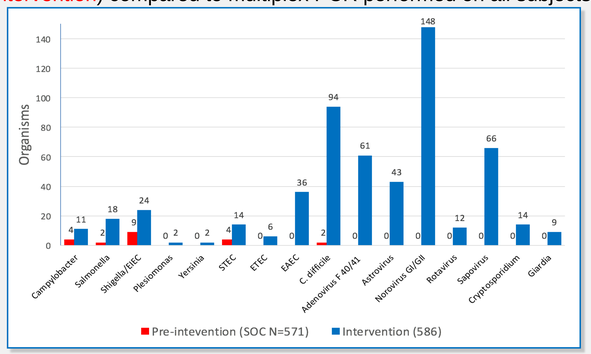
Results

Pathogens detected by ED physicians using standard of care tests, compared to retrospective diagnosis by mPCR in pre-intervention and real time during intervention

	Pre-Intervention Standard of care physician-ordered tests (N=571)	Intervention Standard of care physician-ordered tests (N=586)	Pre-Intervention Multiplex PCR Results blinded to clinician (N=375)	Intervention Multiplex PCR Results available to clinician (N=586)
Campylobacter	4 (0.7%)	1 (0.2%)	13 (3.5%)	11 (2.9%)
Salmonella	2 (0.4%)	6 (1.0%)	11 (2.9%)	18 (3.1%)
Shigella/EIEC	9 (1.6%)	4 (0.8%)	33 (8.8%)	24 (4.1%)*
Plesiomonas			0 (0)	2 (0.3%)
Yersinia			0 (0)	2 (0.3%)
STEC	4 (0.7%)	1 (0.2%)	14 (3.7%)	14 (2.4%)
E. coli O157	4 (0.7%)	1 (0.2%)	3 (0.8%)	3 (0.5%)
ETEC			10 (2.7%)	6 (1.0%)
EAEC			21 (5.6%)	36 (6.1%)
EPEC			76 (20%	67 (11.4%)
C. difficile	2 (0.4%)	6 (0.6%)	43 (11.5%)	94 (16.0%)
C. difficile alone and age ≥ 3years	1 (0.2%)	1 (0.2%)	19 (5.1%)	23 (3.9)*
Adenovirus F 40/41	1 (0.2%)	1 (0.2%)	33 (8.8%)	61 (10.4%)*
Astrovirus			6 (1.6%)	43 (7.3%)
Norovirus GI/GII			57 (15.2%)	148 (25.3%)*
Rotavirus	2 (0.4%)	1 (0.2%)	16 (4.3%)	12 (2.0%)
Sapovirus			31 (8.3%)	66 (11.3%)
Cryptosporidium			10 (2.7%)	14 (2.4%)
Cyclospora			0 (0)	0
Giardia			9 (2.4%)	9 (1.5%)

* P < 0.01 Multiplex PCR prevalence during pre-intervention compared to post-intervention

Figure: Pathogens detected among all subjects with AGE that were available to clinician; physician ordered standard of care tests (pre-intervention) compared to multiplex PCR performed on all subjects

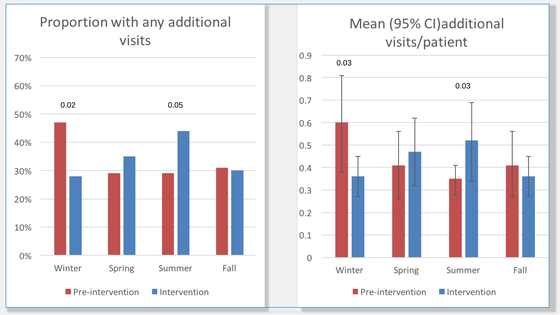


Results

	Pre-Intervention Standard of care physician-ordered tests (N=571)	Intervention Multiplex PCR results available to clinician (N=586)	P-Value
Pathogen identified*	23	434 (74%)	<0.001
Pathogen identified for which treatment generally indicated **	14 (2.5%)	87 (15%)	<0.001
Shigella treated appropriately†	5/33 (15%)	11/24 (46%)	0.06
Pathogen identified for which treatment avoidance is important ††	5 (1%)	32 (5.5%)	<0.001
Any additional visit	174 (30%)	186 (32%)	ns
Mean no. additional visits/subject	0.39	0.40	ns

* Excluding EPEC as clinical implication unclear
* Includes Campylobacter, Shigella, ETEC, C. difficile alone if age >3, Giardia, Cryptosporidium
† Use of azithromycin (15), ciprofloxacin (1),
††Salmonella, STEC

Figure: Proportion returning and return visits by season



Conclusions

- Clinical use of multiplex PCR on stool of all children presenting to ED with acute GE markedly increased detection of treatable pathogens and pathogens (STEC, *Salmonella*) for which antimicrobials should be withheld
- It did not reduce overall return visits to health care providers
- However, multiplex PCR decreased return visits during winter

Limitations

- Periods imbalanced with regard to:
  - Season
  - Viral etiologies
- Children's hospitals with Pediatric ED practitioners, limiting generalizability to other practices
- Not all treatment may have been captured

Next steps

- Mixed effects models, cost analysis, identification of subgroups where multiplex PCR testing is most useful