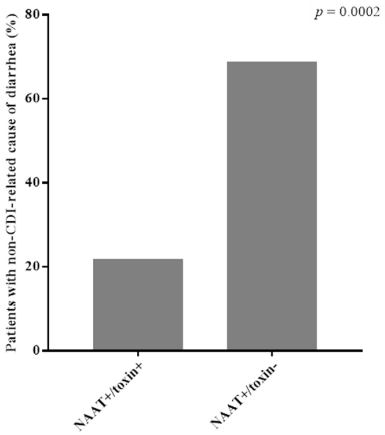

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2357. Toxin Detection Using Single Molecule Counting Technology: The Best of Both Worlds?

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Background. Accurate diagnosis of CDI remains challenging as there is no standalone laboratory test with adequate clinical sensitivity and specificity. Thus, many clinical laboratories currently employ a multistep algorithm incorporating a sensitive screening test followed by a specific toxin test. An automated ultrasensitive toxin immunoassay (Singulex Clarity® *C. difficile* toxins A/B assay) has demonstrated excellent performance compared with cell cytotoxicity neutralization assay (CCNA). In this study, the Clarity assay was evaluated relative to glutamate dehydrogenase (GDH), toxin EIA, toxin B gene PCR, multistep algorithms, and *C. difficile* culture with ribotyping.

Methods. Residual clinical stool samples (n = 293) were collected from patients with suspected CDI. The samples were tested on-site with GDH (*C. DIFF CHEK*™-60), PCR (EntericBio realtime® *C. difficile* assay), a membrane-type toxin EIA (Tox A/B Quik Chek®), and culture and ribotyping. In total, 188 samples were tested with GDH and 239 samples were tested by PCR. All PCR-positive samples (n = 148) and prospectively tested GDH samples (n = 97) were tested with the toxin EIA. Culture and ribotyping information were available for 205 samples.

Results. Three of the samples tested gave no result using the Clarity assay and were excluded from the analysis. The Singulex Clarity *C. difficile* toxins A/B assay had high positive percent agreement (PPA) and low negative percent agreement (NPA) compared with toxin EIA and multistep algorithms ending with toxin EIA. The Clarity assay had high NPA and low PPA compared with PCR, GDH, and the multistep algorithm ending with PCR (figure). Less than 70% of the detected *C. difficile* PCR positive samples had toxins present. There was no difference in toxin concentration between the ribotypes.

Conclusion. The Clarity assay had strong PPA compared with toxin EIA and strong NPA compared with PCR. The low NPA and PPA compared with toxin EIA and PCR, respectively, may reflect the poor sensitivity of current toxin EIAs and low specificity of PCR. The Clarity assay detected 30 different ribotype strains, and less than 70% of samples (by PCR) or strains (by ribotyping) had toxins present. The Clarity assay may be considered for use as a standalone test for CDI diagnosis.

Singulex Clarity C. diff toxins A/B assay	Positive (n)	Negative (n)	Total (n)	Positive percent agreement (95% CI)	Negative percent agreement (95% CI)
GDH → Toxin EIA					
Positive	25	39	64	100 (86.3–100)	75.3 (67.8–81.8)
Negative	0	119	119		
Total	25	158	183		
GDH → Toxin EIA → PCR					
Positive	47	9	56	81.0 (68.6–90.1)	91.7 (84.8–96.1)
Negative	11	99	105		
Total	58	108	166		
PCR → Toxin EIA					
Positive	46	65	111	95.8 (85.7–99.5)	65.4 (58.2–72.2)
Negative	2	123	125		
Total	48	188	236		

Singulex Clarity C. diff toxins A/B assay	Positive (n)	Negative (n)	Total (n)	Positive percent agreement (95% CI)	Negative percent agreement (95% CI)
GDH					
Positive	58	6	64	61.1 (50.5–70.9)	91.9 (83.2–97.0)
Negative	37	68	105		
Total	95	74	169		
PCR					
Positive	102	9	111	69.4 (61.3–76.7)	89.9 (81.7–95.3)
Negative	45	80	125		
Total	147	89	236		
Toxin EIA					
Positive	62	69	131	96.9 (89.2–99.6)	49.6 (41.0–58.3)
Negative	2	68	70		
Total	64	137	201		

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2358. Understanding the Clinical Implications of *Clostridium difficile* Detection in the Molecular Age: Colonization vs. Infection in Children Less Than 3 Years of Age

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Background. Infants have a high rate of asymptomatic *Clostridium difficile* (CD) colonization (up to 37%) but can rarely develop true CD infection (CDI). However, currently available polymerase chain reaction (PCR) and enzyme immunoassays (EIA) have suboptimal sensitivity/specificity to distinguish CDI from colonization. Recent data from adults showed that lower cycle threshold (Ct) values of a semi-quantitative CD toxin B gene (*tcdB*) PCR assay in stool correlated with detection of free CD toxin in stool and poor clinical outcomes. We hypothesized that a *tcdB* PCR assay may be utilized to distinguish CDI from colonization in patients < 3 years old.

Methods. Symptomatic patients < 3 years old with CD detected by the BioFire FilmArray Gastrointestinal Panel (FGP) were enrolled 2/2018–3/2019. We performed CD *tcdB* PCR and toxin A/B/GDH EIA on frozen aliquots of stool in Cary Blair. CDI was defined among those that were *tcdB* PCR positive as (1) a consistent clinical syndrome (diarrhea + no current laxative use), (2) CD EIA toxin+, (3) symptomatic improvement with CDI-directed treatment, and (4) no alternative etiology of diarrhea identified. Patients who did not meet criteria for CDI were considered colonized. We compared median *tcdB* PCR Ct values between the CDI and colonized groups using the Mann–Whitney test.

Results. Of 193 FGP CD+ patient samples with charts available for review, 37 (19%) samples were EIA GDH+/toxin+, 121 (63%) were GDH+/toxin– and 35 (18%) were EIA–. 150 (78%) samples had detectable *tcdB* by PCR. Six (4%) patients met criteria for CDI and 144 (96%) for colonization. Median (interquartile range) *tcdB* PCR Ct values were 23.8 (22.0–29.5) and 30.5 (26.3–35.8) in patients with CDI and colonization, respectively (P = 0.03).

Conclusion. Using a strict clinical and laboratory definition, 4% of evaluable patients < 3 years old met criteria for CDI and had significantly lower *tcdB* PCR Ct values than colonized patients. A combination of clinical and laboratory criteria, including semi-quantitative tcdB PCR, may help differentiate colonization from CDI in this patient population.

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2359. Prospective Feasibility Study for Novel Ultrasensitive Multiplexed Immunoassay for *Clostridiodes difficile* Toxins A and B

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Background. The diagnosis of *Clostridiodes difficile* infection is challenging. A wide array of diagnostic tests are used in practice; however, each available test has important limitations. We examined the feasibility and analytical performance of a novel ultrasensitive multiplexed immunoassay designed by Meso Scale Diagnostics (MSD) compared with five current diagnostic assays for detection of *C. difficile* toxin A and B.

Methods. Stool, serum and urine samples from 44 admitted inpatients were collected within 72 hours of a standard of care nucleic acid amplification test (NAAT) result (23 positive, 21 negative). These specimens underwent five standard diagnostic assays: enzyme immunoassay for toxins A and B (EIA), cytotoxin cell assay, bacterial culture isolation, and two different NAATs to determine presence of viable *C. difficile* cells, toxins, and toxin-encoding genes (Table 1). The concentration (fg/mL) of toxin A and toxin B in all stool samples was then quantified using MSD's multiplexed immunoassay (Table 1).

Results. At least one of the five standard diagnostic tests for *C. difficile* was positive in 16 of the 23 clinically positive patients. The MSD multiplex immunoassay detected toxin A and/or toxin B in 15 of these 16 samples and quantified low levels of toxin A in one clinically positive sample that was negative for all other tests. In contrast, only 2 of the 16 positive samples were positive by EIA, demonstrating the benefits of the ultrasensitive assay over standard immunoassay methods. All clinically negative specimens were negative in all tests. Toxin detection in urine and serum samples was negligible. In stool samples, the MSD test had an estimated sensitivity of 93% (95% CI: 70–99%) and specificity of 93% (95% CI: 78–98%) compared with the clinically used NAAT.

Conclusion. The MSD multiplex toxin assay is a feasible test to move forward for further evaluation. Ultimately, future studies should examine the performance of this test compared with standard of care in a prospective randomized trial assessing clinical outcomes.

Table 1. Diagnostic assay results of study participants.

Diagnosis (Initial NAAT)	Patient Number	Bacterial Culture Result	enolase NAAT	tcdA NAAT (isolate)	tcdB NAAT (isolate)	cdtB NAAT	Clinical GeneXpert (NAAT) Result	Cytotoxicity Result	EIA Result	MSD Toxin A Results	MSD Toxin B Results
Positive	Patient 1	+	+	+	+	-	+	+	+	+	+
Positive	Patient 2	-					+	-	-	+	-
Positive	Patient 3	+	+	+	+	-	+	-	-	+	-
Positive	Patient 4	+	+	+	+	-	+	-	-	-	+
Positive	Patient 5	-					-	-	-	-	-
Positive	Patient 6	+	+	+	+	-	+	+	+	+	+
Positive	Patient 7	+	+	+	+	-	+	-	-	+	+
Positive	Patient 8	-					+	+	-	-	+
Positive	Patient 9	-					-	-	-	+	-
Positive	Patient 10	-					-	-	-	-	-
Positive	Patient 11	-					-	+	-	-	+
Positive	Patient 12	+	+	+	+	-	+	+	-	+	+
Positive	Patient 13	-					-	-	-	-	-
Positive	Patient 14	-					-	-	-	-	-
Positive	Patient 15	-					+	+	-	+	+
Positive	Patient 16	-					-	-	-	-	-
Positive	Patient 17	+	+	+	+	-	+	-	-	-	-
Positive	Patient 18	+	+	+	+	-	+	-	-	+	+
Positive	Patient 19	-					+	+	-	+	+
Positive	Patient 20	-					-	-	-	-	-
Positive	Patient 21	+	+	+	+	+	+	+	-	+	+
Positive	Patient 22	-					+	-	-	+	-
Positive	Patient 23	+	+	+	+	+	+	-	-	-	+
Negative	Patient 24	-					-	-	-	-	-
Negative	Patient 25	-					-	-	-	-	-
Negative	Patient 26	-					-	-	-	-	-
Negative	Patient 27	-	+	-	-	-	-	-	-	-	-
Negative	Patient 28	-					-	-	-	-	-
Negative	Patient 29	-					-	-	-	-	-
Negative	Patient 30	-					-	-	-	-	-
Negative	Patient 31	-					-	-	-	-	-
Negative	Patient 32	-					-	-	-	-	-
Negative	Patient 33	-					-	-	-	-	-
Negative	Patient 34	-					-	-	-	-	-
Negative	Patient 35	-					-	-	-	-	-
Negative	Patient 36	-					-	-	-	-	-
Negative	Patient 37	-					-	-	-	-	-
Negative	Patient 38	-	+	-	-	-	-	-	-	-	-
Negative	Patient 39	-					-	-	-	-	-
Negative	Patient 40	-					-	-	-	-	-
Negative	Patient 41	-					-	-	-	-	-
Negative	Patient 42	-					-	-	-	-	-
Negative	Patient 43	-					-	-	-	-	-
Negative	Patient 44	-					-	-	-	-	-

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2360. Impact of a Two-Step Antimicrobial Stewardship Intervention on *C. difficile* Infection Diagnosis at an Urban Veteran's Affairs Medical Center

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Background. *C. difficile* infection (CDI) is a common healthcare-associated infection and quality measure for hospitals. Diagnosis of CDI is challenging as testing modalities, i.e., nucleic acid amplification test (NAAT), are highly sensitive but cannot differentiate between colonization and infection. Therefore, judicious use of testing is critical to avoid unnecessary diagnosis and treatments.

Methods. This single-center, retrospective chart review evaluated the impact of a two-step diagnostic stewardship intervention on *C. difficile* diagnosis and use of oral vancomycin in the inpatient setting. For the first step of the intervention, providers were educated on appropriate diagnosis and treatment, and given access to an optional electronic CDI clinical decision support system (CDSS). For the second step of the intervention, the CDI NAAT stand-alone testing option was removed from the lab ordering menu and providers were required to use the CDSS to order testing. Clinical data including bed-days of care (BDOC), total number tests ordered, number of positive tests and use of oral vancomycin was collected for the pre-intervention period (1/1/16 – 3/31/17), post intervention period 1 (April 1, 2017–October 31/18) and post-intervention period 2 (November 1, 2018–March 31, 2019).

Results. Compared with the pre-intervention group, there were no significant differences in the number of total CDI NAATs ordered, positive CDI NAATs or vancomycin DOT/10,000 BDOC in post-intervention group 1. There was a reduction in the number of total CDI NAATs ordered (341 vs. 42 [87.7%]) and the number of positive CDI NAATs (56 vs. 7 [87.5%]) in post-intervention group 2, respectively. When this data were normalized based on bed days of care (BDOC), there were still significant reductions in NAATs ordered and number of positive CDI NAATs (64 vs. 27 [57.8%]; 11 vs. 5, respectively, [54.5%]) and with vancomycin oral DOT/10,000 BDOC (72 vs. 7 [90.3%]) (Table 1).

Conclusion. Provider education and an optional CDSS did not significantly impact CDI NAAT ordering or use of oral vancomycin for CDI. However, implementation of a mandatory CDSS for CDI testing was shown to significantly decrease the number of tests ordered, the number of positive tests, and the use of oral vancomycin.

Table 1: CDI NAATs[1], Vancomycin DOT[2]/10,000 BDOC[3]: Pre-Intervention vs. Post Intervention Periods 1&2

Groups / Dates	BDOC (days)	Total NAATs	Positive NAATs	Total NAATs/10,000 BDOC	Positive NAATs/10,000 BDOC	Vancomycin Oral DOT/10,000 BDOC
Pre-Intervention Group: 1/1/16 to 3/31/17	53,015	341	56	64	11	72
Post Intervention Period 1: 4/1/17 - 10/31/18	61,048	362	70	59	11	62
Post Intervention Period 2: 11/1/18 - 3/31/19	15,445	42	7	27	5	7

1. *C. difficile* infection nucleic acid amplification test
2. Days of Therapy
3. Bed Days of Care

Disclosures. **All authors:** No reported disclosures.

2361. Evaluation of a 2-Step Testing Algorithm for *Clostridioides difficile* Infection

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Background. Clinical data describing use of a multistep algorithm for diagnosis of *Clostridioides difficile* infection (CDI) is limited. In June 2018 we implemented a 2-step testing algorithm in which PCR testing (Aries® assay) is performed for all specimens followed by EIA toxin testing (TOX A/B QUIK CHEK® assay) when PCR is positive. We sought to describe outcomes for patients with PCR+/EIA+ vs. PCR+/EIA– results. Outcomes evaluated included frequency of CDI treatment, retesting and retreatment within 3 months, and investigator determined categorization of *C. difficile* results by an investigator blinded to the EIA result.

Methods. A retrospective cohort study was performed on a random sample of 85 unique patients with a PCR+ stool sample from July 2018 through December 2018. Demographic and clinical data were abstracted from the medical record during the index encounter and for 3 months thereafter. Based on predetermined criteria, index encounter results were categorized as representing probable, possible, unlikely, or indeterminate cases of symptomatic CDI.

Results. For the 85 study patients, 42%, 27%, and 31% were tested in the inpatient, outpatient, and ED/urgent care settings. Twenty-seven patients (32%) were EIA+, all of whom received CDI treatment. Fifty-eight (68%) were EIA-, of which 79% received treatment. Of the 12 EIA- patient who did not receive treatment two had retesting within 3 months; one of whom subsequently tested EIA+ and was treated and the other tested PCR-. At least 1 *C. difficile* test was repeated within 3 months in 48% of EIA+ and 33% of EIA- patients. Based on repeat testing CDI treatment was prescribed for 12% of EIA+ subjects and for 11% of EIA- subjects. For the EIA+ patients, 70%, 19%, 7%, and 4% were classified as probable, possible, unlikely and indeterminate cases of symptomatic CDI when compared with 38%, 34%, 22%, and 5% for EIA- patients.

Conclusion. During the first 6 months of a 2-step testing algorithm, we found that patients with EIA- test results were frequently treated for CDI and that 72% of EIA- cases were classified as probably or possibly having symptomatic CDI. Further study is needed to determine whether patients with EIA- results categorized with probable or possible symptomatic CDI would improve without CDI treatment.

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2362. Back to the Future: The Impact of Multi-Step Algorithm *C. difficile* Testing at a Large Tertiary Medical Center

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Background. Antibiotic stewardship and infection control programs rely on *C. difficile* infection (CDI) test results to measure CDI incidence in the hospital setting. *C. difficile* carriage is common and distinguishing infection from colonization is difficult with the highly sensitive nucleic acid amplification testing (NAAT) commonly used. Current guidelines recommend a multi-step algorithm for testing. The impact on patient outcomes and CDI metrics are largely unknown.