Background. Commercially available tests for Clostridium difficile infection (CDI) make test selection by the laboratory difficult due to the following unsatisfactory characteristics: long turnaround time, poor sensitivity, and/or poor specificity. The Singulex Clarity® C. diff toxins A/B assay (in development) is a rapid and automated immunoassay for the detection of C. difficile toxins A and B in stool, with limits of detection for toxins A and B at 2.0 and 0.7 pg/mL, respectively. In this multi-center study, the clinical performance of the Singulex Clarity C. diff toxins A/B assay was compared with standalone PCR, a multistep algorithm with enzyme immunnoassay (EIA) and PCR, and cell cytotoxicity neutralization assay (CCNA).

Methods. Fresh samples from 267 subjects with suspected CDI were tested at two sites (Minneapolis Medical Research Foundation and TriCore Reference Laboratories) with the Singulex Clarity assay, PCR (Xperi C. difficile), and EIA (C. Diff Quik Chek Complete®) for GDH and toxin testing. The performance of the assays and multistep algorithms were evaluated against CCNA (Microbiology Specialists, Inc.).

Results. The overall CDI prevalence was 15.7%. The Singulex Clarity C. diff toxins A/B assay had 90.5% sensitivity and 96.0% specificity, with a 98.2% negative predictive value when compared with CCNA, and the Clarity assay's AuROC was 0.9534, PCR had 90.3% sensitivity and 91.1% specificity. Compared with CCNA, the toxin EIA had 47.6% sensitivity and 100% specificity. Testing with a multistep algorithm using EIA with discordant results reflected to PCR resulted in 85.7% sensitivity and 94.7% specificity.

Conclusion. The ultrasensitive Singulex Clarity C. diff toxins A/B assay is equivalent to the sensitivity of PCR while providing higher specificity. Compared with a multistep algorithm, the Clarity assay provides higher sensitivity and specificity while providing faster time-to-result in a simpler-to-understand, one-step reporting structure that provides a single-step solution for detection of C. difficile toxins in patients with suspected CDI.

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1089. Analytical Performance of an Ultrainsensitive Immunoassay for Detection of Clostridium difficile Toxins in Stool

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Background. Clostridium difficile infection (CDI) is the main cause for nosocomial diarrhea. Currently available assays for the diagnosis of CDI show deficits in sensitivity, specificity, and/or turnaround time. The Singulex Clarity® C. diff toxins A/B assay, in development for the Singulex Clarity® system, was designed to provide an accurate and automated detection of C. difficile toxins A (TcdA) and B (TcdB) in stool. Here, the analytical performance of the assay is reported.

Methods. Limit of detection (LoD) for TcdA and TcdB in stool and buffer was determined, and a preliminary cutoff was defined after testing with cell cytotoxicity neutralization assay (CCNA). Sensitivity was studied by analytical activity and toxigenic and nontoxigenic C. difficile strains of eight different toxinootypes was determined. Cross-reactivity was analyzed for 53 other gastrointestinal pathogens and potential interference by 11 endogenous and exogenous substances were determined. Reproducibility was tested with triplicate samples (n = 85), and stability was evaluated in samples stored at room temperature, refrigerated, and frozen conditions, and subjected to three freeze-thaw cycles.

Results. The LoDs for TcdA and TcdB were 0.8 and 0.3 pg/mL in buffer, and 2.0 and 0.7 pg/mL in stool, respectively. Using a preliminary cutoff, the assay demonstrated 96.3% sensitivity and 96.1% specificity compared with CCNA. The Singulex Clarity® C. diff toxins A/B assay detected toxins from all tested strains and toxinootypes. No cross-reactivity or interference were detected. The repeatability was 99%, and samples for C. difficile toxin testing were stable up to 8 hours in room temperature, 1 week in 2–8°C, 6 months in −70°C, and up to three freeze-thaw cycles.

Conclusion. The Singulex Clarity C. diff toxins A/B assay (in development) can detect TcdA and TcdB at very low concentrations and it has high sensitivity and specificity compared with CCNA. The assay demonstrates reactivity to common C. difficile strains, does not show cross-reactivity to common gastrointestinal pathogens, is robust against common interferents, allows for toxin detection in both fresh and frozen stool samples and up to three freeze-thaw cycles, and provides results with high reproducibility.

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1090. Patient Outcomes With Prevented vs. Negative Clostridium difficile Tests Using Computerized Clinical Decision Support (CCDS)

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Background. Overtesting and overdiagnosis of Clostridium difficile infection (CDI) are increasingly recognized as potentially avoidable causes for unnecessary inappropriate testing and/or treatment, with associated increased cost. Reducing inappropriate testing through diagnostic stewardship may improve C. difficile test utilization. However, the safety of these interventions is not well understood, despite the potential risk for missed or delayed diagnosis. A computerized clinical decision support (CCDS) tool was implemented at a 619-bed tertiary care hospital as part of a multifaceted effort to reduce inappropriate C. difficile testing. The intervention was associated with reductions in tests (41%) and hospital-onset CDI events (31%). We sought to examine patient outcomes associated with the intervention.

Methods. The CCDS was designed to identify patients with a prevented test if a provider initiated the CCDS and aborted the order. Outcomes of patients with either a prevented or negative nuclear acid amplification test (NAAT) were compared retrospectively. A logistic regression model was created to evaluate the association between a prevented test attempt and serious adverse events. Patients with a subsequent positive result within 7 days of the initial trigger and those treated with CDI-effective antibiotics underwent chart review.

Results. Multivariate analysis of 637 cases (490 negative, 147 prevented) showed that a prevented test was not associated with the primary composite outcome (inpatient mortality or ICU-transfer) compared with a negative test (adjusted odds ratio, 0.912; 95% CI 0.513–1.571). Prevented tests were associated with shorter length of stay and similar rates of CDI-related complications. Eleven (7.5%) had a subsequent positive CDI, four within 30 minutes of the prevented test, suggesting nonsignificant delay in testing. Of the remaining seven patients, case review failed. S. Biscet five did not meet testing criteria while two met testing criteria at the time of the prevented test. No serious adverse events attributable to delayed CDI diagnoses or unjustified CDI treatment were identified by individual case review.

Conclusion. CCDS-based diagnostic stewardship for CDI may be both a safe and effective means to reduce inappropriate testing.

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1091. Algorithmic Release of Clostridium difficile PCR Results From a Multiplex Gastrointestinal (GI) Panel in Children <3 Years Old

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Background. Infants have a high rate of asymptomatic Clostridium difficile (CD) colonization, up to 37%. Given this, our laboratory does not release CD+ results from the BioFire FilmArray Gastrointestinal Panel (FGP) in patients <3 years, unless requested by a physician. We sought to validate this model by comparing results from FGP to semi-quantitative CD PCRs for toxin B and glutamate dehydrogenase (GDH), enzyme immunoassay (EIA) for toxin A/B/GDH, and physician requests for CD results.

Methods. Retrospective analysis of children <3 years with GI illness and FGP CD+ results between September 2016 and April 2018. CD PCRs for toxin B and GDH, CD EIA for toxin A/B/GDH were performed on convenience samples of frozen aliquots in Cary Blair. Physician request for release of CD results was used as a surrogate of possible role of CD on GI illness.

Results. Of 5,990 FGP 2,267 (38%) were in children <3 years: 619 (27%) were CD+. Of these 619, 602 (97%) were not reported per algorithm. 62% (386/619) of CD+ samples had co-pathogens detected; enteropathogenic Escherichia coli and norovirus most frequently. For CD PCRs and EIA performed in subset of 49 CD+, toxin B and GDH threshold values (Cts) were evaluated (Table 1). Of samples with detectable CD toxin B PCR, 14 (29%) had both GDH and toxin B detected, 24 (51%) had only GDH detected, and 9 (19%) had neither GDH nor toxin B detected.

Conclusion. Only 3% of FGP CD+ results in children <3 years were released per physician request, suggesting limited clinical significance. A co-pathogen was detected in 62% of CD+ samples that may explain illness. Among evaluable samples, only 28.6% of CD+ had both GDH and toxin detected by EIA, possibly indicating low specificity of CD detection by EIA. Prospective studies are warranted to determine the validity of our algorithm and if semi-quantitative PCR or EIA can be useful to identify when CD detection by FGP in children <3 years is clinically significant.

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