1-1-2020

# Evaluating Appropriateness and Diagnostic Stewardship Opportunities of Multiplex Polymerase Chain Reaction Gastrointestinal Testing Within a Hospital System

Melissa O'Neal
*University of South Carolina - Columbia*

Hanna Murray
*University of South Carolina - Columbia*

Sangita Dash
*University of South Carolina School of Medicine*

Majdi N. Al-Hasan
*University of South Carolina School of Medicine*

Julie Ann Justo
*University of South Carolina - Columbia*, justoj@cop.sc.edu



## Publication Info

Published in *Therapeutic Advances in Infectious Disease*, Volume 7, 2020, pages 2049936120959561-.

Author(s)
Melissa O'Neal, Hanna Murray, Sangita Dash, Majdi N. Al-Hasan, Julie Ann Justo, and P Brandon Bookstaver

Therapeutic Advances in Infectious Disease Original Research

# Evaluating appropriateness and diagnostic stewardship opportunities of multiplex polymerase chain reaction gastrointestinal testing within a hospital system

*Ther Adv Infectious Dis*

2020, Vol. 7: 1–10

DOI: 10.1177/2049936120959561



**Melissa O'Neal, Hanna Murray, Sangita Dash, Majdi N. Al-Hasan, Julie Ann Justo and P. Brandon Bookstaver**

***Abstract***

**Objective:** This single-center, retrospective, observational cohort study evaluates the appropriateness of the BioFire® FilmArray® Gastrointestinal (GI) multiplex PCR panel testing at a community-teaching hospital.

**Methods:** All adult, hospitalized patients at Prisma Health Richland Hospital with a documented GI multiplex PCR panel from 1 April 2015 through 28 February 2018 were included in the analysis. Inappropriate use of the GI panel was defined as a test obtained without documented diarrhea, greater than 2 days of hospitalization, redundant use with other diagnostic tests (e.g. *Clostridioides difficile* PCR), or laxative use in the preceding 48 h. Antibiotic use and host variables were compared between groups with positive and negative results.

**Results:** During the study period, 442 GI panels were obtained, among which 268 (61%) were deemed inappropriate. Primary reasons for inappropriate testing were lack of documented diarrhea ($n = 92$), greater than 2 days of hospitalization ($n = 116$), having a duplicate *C. difficile* PCR test ordered ($n = 118$), or laxative use in the 48 h before testing ($n = 36$). A total of 141 (32%) GI panels were positive. The most frequently identified pathogens were *C. difficile* (51.1%, $n = 72$), Enteropathogenic *Escherichia coli* (17.7%, $n = 25$), and Norovirus GI/GII (12.1%, $n = 17$). Patients with negative GI panel results were initiated on antibiotics significantly less frequently than those with positive GI panels (62.5% *versus* 80.2%, $p < 0.00001$).

**Conclusion:** Stewardship opportunities exist to optimize the diagnostic application of the GI multiplex PCR panel.

***Keywords:*** *Clostridioides difficile*, multiplex polymerase chain reaction, diagnostic stewardship, antimicrobial stewardship, infectious diarrhea

Received: 3 July 2020; revised manuscript accepted: 27 August 2020.

Correspondence to:
**P. Brandon Bookstaver**
University of South Carolina College of Pharmacy, 715 Sumter Street, Columbia, SC 29208, USA

Prisma Health Richland Hospital, 5 Richland Medical Park Drive, Columbia, SC 29203, USA
**bookstaver@cop.sc.edu**

**Melissa O'Neal**
University of South Carolina College of Pharmacy, 715 Sumter Street, Columbia, SC 29208, USA
**mponeal@email.sc.edu**

**Hanna Murray**
University of South Carolina College of Pharmacy, Columbia, SC, USA

**Sangita Dash**
**Majdi N. Al-Hasan**
University of South Carolina School of Medicine, Columbia, SC, USA

Prisma Health Richland Hospital, Columbia, SC, USA

**Julie Ann Justo**
University of South Carolina College of Pharmacy, Columbia, SC, USA

Prisma Health Richland Hospital, Columbia, SC, USA

## Introduction

Since its development, application of polymerase chain reaction (PCR) technology has transitioned from genome projects and forensics to the expeditious and rapid identification of infectious diseases.[1] The BioFire® FilmArray® Gastrointestinal (GI) panel uses multiplex PCR technology for the rapid detection of 22 pathogens causing infectious diarrhea.[2] The pathogens recognized on this panel are typically community-acquired, including several *Escherichia coli* pathotypes, additional bacteria, viruses, and gastrointestinal parasites. *Clostridioides difficile* (toxin A/B) is also included in the GI panel. Although historically considered a nosocomial pathogen, community-acquired cases of *C. difficile* infection (CDI) have surpassed hospital and healthcare associated cases in South Carolina,[3] and represent roughly one-half of cases nationally.[4] With this comprehensive diagnostic tool, results are available approximately 60 min after sample processing in the laboratory, with a reported 98.5% sensitivity and 99.2% specificity.[2]

Use allows for earlier administration of appropriate anti-infective therapy, and has been shown to reduce hospital length of stay and, importantly, additional diagnostic testing.[5]

While the results of this panel directly influence patient care, they also impact various benchmarks used to determine effectiveness of several hospital departments. Antimicrobial stewardship programs are assessed using metrics such as incidence rates of hospital-onset CDI, multi-drug resistant bacteria, appropriateness of empiric and definitive anti-infective therapy, and cost containment.[6] These measurable outcomes are important to determine the quality of stewardship initiatives. Similarly, in response to panel results, a hospital's infection control and prevention program will evaluate hospital-onset infections, and adherence to protocols including contact precautions and appropriate hand hygiene. With these rapid diagnostics housed in the microbiology laboratory, the microbiology department has jurisdiction over the execution of the test and reporting of results. Thus, GI panel results impact interdepartmental shared metrics, making awareness and collaboration key to optimizing patient care.[6]

The concept of diagnostic stewardship is used to offer organized guidelines for appropriate use of these rapid diagnostics and improved application to patient care. This includes guidance on identifying relevant patient populations for testing, as well as education on the nuances of newer technologies. A survey of stewardship pharmacists' familiarity with rapid diagnostic technologies indicated multiplex PCR are the most commonly utilized tests but least familiar among respondents.[7] This, along with the increasing use of multiplex panels, leaves room for significant educational intervention, and highlights the need for diagnostic stewardship to ensure optimal use of next generation rapid diagnostics.

This study evaluates appropriateness of the BioFire® FilmArray® GI panel (referred to as GI panel throughout) ordering at a large, community-teaching hospital to identify current demographic, temporal, and epidemiological trends from descriptive data. These results will be used to guide local recommendations for diagnostic stewardship measures.

## Methods

### Study population

This study was conducted at Prisma Health Richland, a 641-bed, community-teaching medical center (Columbia, SC, USA). All admitted patients over the age of 18, who had the GI panel conducted between 1 April 2015 and 28 February 2018 were included for analysis. Patients with prolonged hospitalizations who had the GI panel run more than once were entered as a new encounter for each use of the test. Anyone under the age of 18 or outpatients at the time of testing were excluded.

The primary objective of this study was to determine appropriateness of GI panel testing. An encounter was deemed "inappropriate" if it met any of the following criteria: no reported or documented diarrhea, greater than 2 days of hospitalization prior to sample collection, concomitant or *post hoc* singleplex Xpert® *C. difficile* PCR, or laxative use in preceding 48 h of sample collection. Antibiotic use was compared between patients with positive and negative GI panel results.

### FilmArray GI panel

The GI panel tests for *Campylobacter* spp. (*jejuni, coli* and *upsaliensis*), *Clostridioides difficile* (toxin A/B), *Plesiomonas shigelloides*, *Salmonella, Yersinia enterocolitica, Vibrio* spp. (*parahaemolyticus, vulnificus* and *cholerae*), *Vibrio cholerae*, Enteroaggregative *E. coli* (EAEC), Enteropathogenic *E. coli* (EPEC), Enterotoxigenic *E. coli* (ETEC) lt/st, Shiga-like toxin-producing *E. coli* (STEC) stx1/stx2, *E. coli* O157, *Shigella*/Enteroinvasive *E. coli* (EIEC), Adenovirus F40/41, Astrovirus, Norovirus GI/GII, Rotavirus A, Sapovirus (I, II, IV, and V), *Cryptosporidium, Cyclospora cayetanensis, Entamoeba histolytica*, and *Giardia lamblia*. The assay was performed according to the manufacturer's instructions and results were released to the electronic health record (EHR).

### Data and statistics

Data were collected from the EHRs after de-identification and entered using REDCap®. Descriptive statistics, frequency tables, and charts were used to summarize the data using Microsoft Excel® 2007 (16.0.13029.20232). Quarterly increase in use of test was assessed using a single-factor

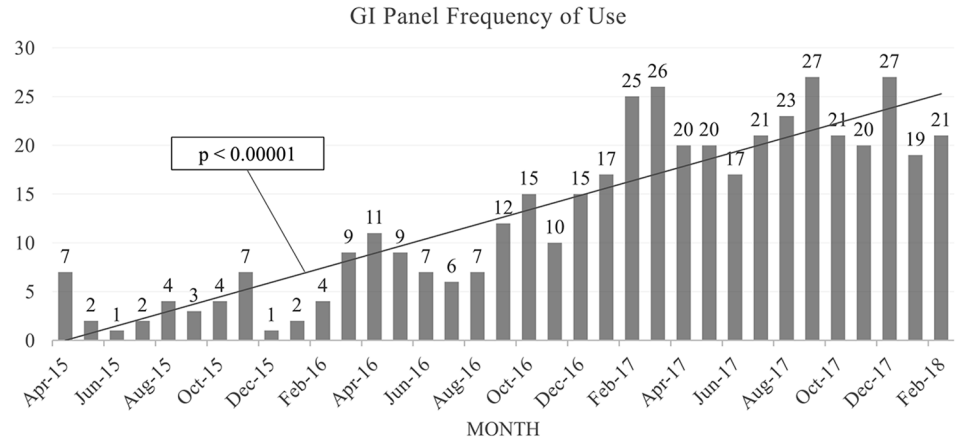


**Figure 1.** GI panel frequency of use. A total of 442 encounters occurred over the 35-month period.
GI panel, BioFire® Gastrointestinal panel.

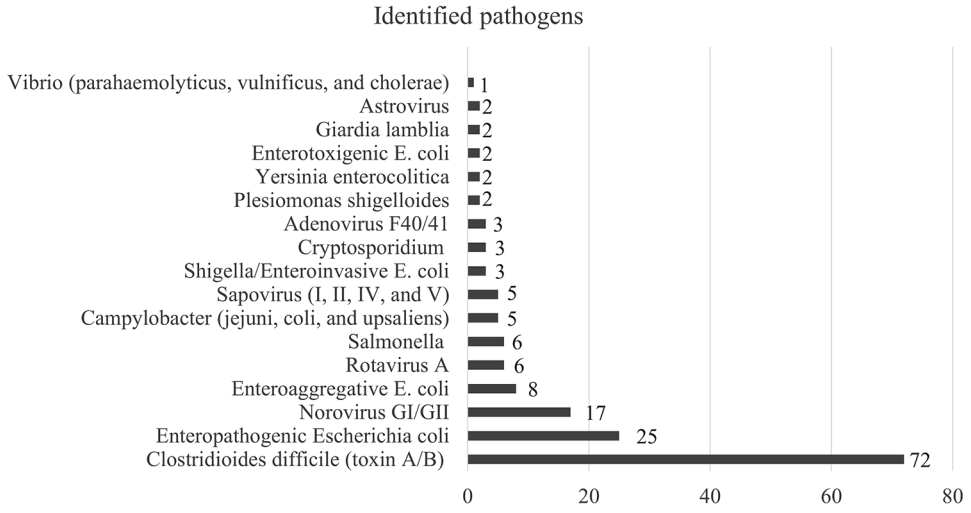


**Figure 2.** Identified pathogens. There were 141 cases with positive test results, and the most commonly identified pathogen was *Clostridioides difficile* Toxin A/B.

ANOVA. Antibiotic use and host factors were compared between patients with positive and negative multiplex PCR results, respectively, using chi-square test.

This study was approved as an exempt review by the IRB of Prisma Health-Midlands (Pro00050721). Due to the retrospective nature of this study, a waiver of informed consent was granted.

## Results

Among the GI panels screened during the study period, 442 were included for assessment. There was a temporal increase in use of the GI panel over time as demonstrated in Figure 1 ($p < 0.00001$).

Of the 442 uses, 141 yielded positive results (31.9%). The most common pathogens identified were *C. difficile* toxin A/B (72/141, 51.1%), EPEC (25/141, 17.7%), and Norovirus GI/GII (17/141, 12.1%). Figure 2 shows the prevalence of all pathogens identified in this study. In 20/141 (14.2%) cases, more than one pathogen was detected, and the greatest number of pathogens detected in a single sample was four (*Vibrio* spp., EAEC, EPEC, and Norovirus were all detected in one panel).

**Table 1.** Baseline characteristics.

| Variable | Total ($n=442$) | Positive test ($n=141$) | Negative test ($n=301$) |
|---|---|---|---|
| Age, years, mean (SD) | 57 (18.1) | 56 (18.6) | 57.7 (17.9) |
| Sex, male, *n* (%) | 237 (53.6) | 80 (56.7) | 157 (52.2) |
| Race/Ethnicity *n* (%) | | | |
| African American | 232 (52.5) | 62 (44.0) | 170 (56.5) |
| Caucasian | 192 (43.4) | 71 (50.4) | 121 (40.2) |
| Hispanic | 8 (1.8) | 3 (2.1) | 5 (1.7) |
| Asian | 3 (0.7) | 2 (1.4) | 1 (0.3) |
| Other | 9 (2.0) | 3 (2.1) | 6 (2.0) |
| HIV positive, *n* (%) | 35 (7.9) | 13 (9.2) | 22 (7.3) |
| Active cancer, *n* (%) | 21 (4.8) | 5 (3.5) | 16 (5.3) |
| Chronic GI disorder, *n* (%) | 81 (18.3) | 22 (15.6) | 59 (19.6) |
| Acute diarrhea[x], *n* (%)♦ | 311 (70.4) | 111 (78.7) | 200 (66.4) |
| Liver cirrhosis, *n* (%) | 36 (8.1) | 12 (8.5) | 24 (8.0) |
| Diabetes, *n* (%) | 159 (36.0) | 49 (34.8) | 110 (36.5) |
| Recent hospitalization[†], *n* (%) | 157 (35.5) | 43 (30.5) | 114 (37.9) |
| Recent GI surgery*, *n* (%) | 12 (2.7) | 3 (2.1) | 9 (3.0) |
| Prior antibiotic exposure[†], *n* (%) | 184 (41.6) | 53 (37.6) | 131 (43.5) |
| Use of immunosuppressants[†], *n* (%) | 30 (6.8) | 10 (7.1) | 20 (6.6) |

[†]⩾48 h duration within preceding 90 days.
*Within preceding 30 days.
[x]Excludes chronic diarrhea (⩾28 days).
♦Indicates $p \leqslant 0.05$.
GI, gastrointestinal; HIV, human immunodeficiency virus; SD, standard deviation.

Pathogens on the panel that were not detected during the study period included *Vibrio cholerae*, Shiga-like toxin-producing *E. coli*, *E. coli* O157, *Cyclospora cayetanensis*, and *Entamoeba histolytica*.

Baseline and clinical characteristics are outlined in Tables 1 and 2, respectively. The mean age was 57 years and the majority of patients were male (53.6%). The panel was run early in admission for most patients, with 74.2% of tests being run within the first 48 h of admission. Of the 442 records, 91 (20.6%) met qSOFA (quick sepsis-related organ failure assessment) criteria for sepsis. There was a greater proportion of patients with positive GI panels experiencing acute diarrhea than those with negative results (78.7% *versus* 66.4%, $p < 0.00001$). Recent hospitalization was higher in patients with negative panels (37.9%) than in patients with positive panels (30.5%), but the difference was not significant. The proportion of patients who received tube feeds was significantly higher in those with negative GI panels (1.4% *versus* 8.3% $p < 0.00001$). Probiotic use was also significantly higher in this population (2.1% *versus* 8.0%, $p = 0.017$). A total of three patients had the panel run a second time, and 118 (26.7%) had a concomitant separate *C. difficile* PCR. Prior antibiotic exposure of at least 48 h duration in the preceding 90 days was confirmed in 184 cases (41.6%). Overall, the

**Table 2.** Clinical characteristics.

| Variable | Total ($n=442$) | Positive test ($n=141$) | Negative test ($n=301$) |
|---|---|---|---|
| Test conducted on hospital day ⩽2, *n* (%) | 328 (74.2) | 112 (79.4) | 216 (71.8) |
| qSOFA ⩾2, *n* (%) | 91 (20.6) | 32 (22.7) | 59 (19.6) |
| Concomitant or *post hoc Clostridioides difficile* PCR, *n* (%) | 118 (26.7) | 39 (27.7) | 79 (26.2) |
| Repeat GI panel, *n* (%) | 3 (0.7) | 1 (0.7) | 2 (0.7) |
| Separate O&P, *n* (%) | 70 (15.8) | 23 (16.3) | 47 (15.6) |
| Separate stool culture, *n* (%) | 153 (34.6) | 56 (39.7) | 97 (32.2) |
| Concurrent PEG tube, *n* (%) | 16 (3.6) | 3 (2.1) | 13 (4.3) |
| Tube feeds‡, *n* (%)♦ | 27 (6.1) | 2 (1.4) | 25 (8.3) |
| Laxative use‡, *n* (%) | 36 (8.1) | 14 (9.9) | 22 (7.3) |
| Stool softener use‡, *n* (%) | 44 (10.0) | 17 (12.1) | 27 (9.0) |
| PPI use‡, *n* (%) | 181 (41.0) | 56 (39.7) | 125 (41.5) |
| H2 use‡, *n* (%) | 49 (11.1) | 14 (9.9) | 35 (11.6) |
| Probiotic use‡, *n* (%)♦ | 27 (6.1) | 3 (2.1) | 24 (8.0) |

‡Presumed or documented use in preceding 48 h.
♦Indicates $p \leqslant 0.05$.
GI, gastrointestinal; qSOFA, quick sepsis-related organ failure assessment; O&P, ova and parasite; PCR, polymerase chain reaction; PEG, percutaneous endoscopic gastrostomy; PPI, proton pump inhibitor; H2, H2 receptor antagonist; SD, standard deviation.

most common agents with prior exposure were vancomycin (38.3%), ceftriaxone (27.3%), and metronidazole (24.6%).

### *Inappropriate use*

There were a total of 268 records that met "inappropriate" use criteria, as displayed in Figure 3. The most common reasons were tests conducted after more than 2 days of hospitalization ($n=116$), and use of the *C. difficile* toxin B PCR in addition to the GI panel ($n=118$). Among the 118 records that had both the GI panel and the *C. difficile* PCR, 87 records (73.7%) had both tests run from the same stool sample. The majority of inappropriate testing had a negative GI panel result (188/268, 70.1%). Lack of reported or documented diarrhea was significantly higher in patients with negative GI panels ($p=0.009$); all other criteria were not significantly different between appropriate and inappropriate uses of the test.

There were 72 records with positive GI panels indicating *C. difficile* toxin A/B. Concomitantly identified pathogens included *Campylobacter* spp. ($n=2$), Enteropathogenic *E. coli* ($n=5$), *Cryptosporidium* ($n=1$), Norovirus GI/GII ($n=2$), and Sapovirus ($n=1$). Of the 72 positive panels for *C. difficile*, 18 also had an additional *C. difficile* PCR test run. Of note, 15/18 (83.3%) had both tests run on the same stool sample. In two cases, the GI panel detected *C. difficile*, but the individual *C. difficile* PCR did not.

Among the 72 positive panels for *C. difficile*, 28 (38.9%) had a recent hospitalization, 34 (47.2%) had confirmed or suspected use of a proton pump inhibitor, and 31 (43.1%) had prior antibiotic exposure. Median duration of reported diarrhea was 2 days [interquartile range (IQR): 6.5 days]. The longest duration of diarrhea reported was 60 days. Mean white blood cell count was 11,400 cells/μl (±8160 cells/μl). The most common antibiotics used post-test were metronidazole

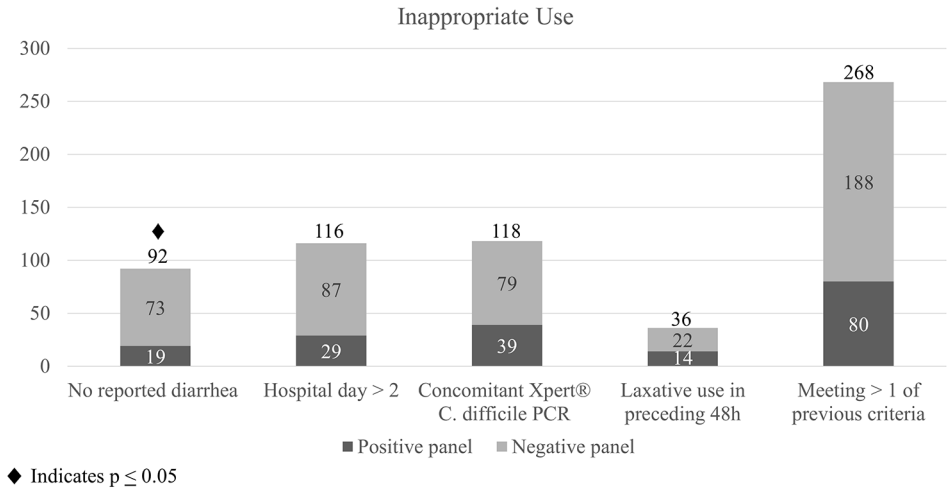


**Figure 3.** Inappropriate use. A total of 268 encounters met at least one of the inappropriate use criteria. Values reported are absolute numbers.
PCR, polymerase chain reaction.

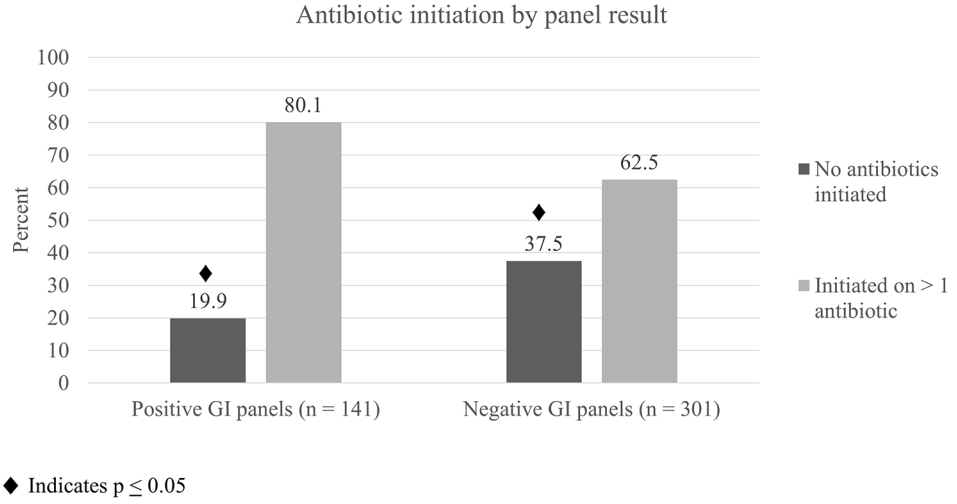


**Figure 4.** Post-test antibiotic initiation by panel result. Antibiotics were not used post test in 19.8% of cases with positive panel results *versus* 37.5% of cases with negative panel results.
GI panel, BioFire® Gastrointestinal panel.

(55/72, 76.4%), and/or oral vancomycin (39/72, 54.2%).

### *Impact on antibiotic therapy*

Use of post-test antibiotics and duration of therapy were recorded (Figure 4). There were 28/141 (19.9%) patients with positive GI panels not initiated on antibiotics post test, compared with 113/301 (37.5%) in patients with negative GI panels ($p < 0.00001$).

Mean days of therapy (DOT) for the first three antibiotics used post test in all cases was 5.1 days; those with positive panels had an average DOT of 5.4 days *versus* 4.8 days in those with negative panels. Frequency of use for antibiotics used in greater than 5% of patients, as well as average duration is delineated for positive and negative panels in Figures 5 and 6. The agents most frequently used in patients with positive GI panels were metronidazole (48.9%), oral vancomycin (27.7%), and ciprofloxacin (16.3%). The most

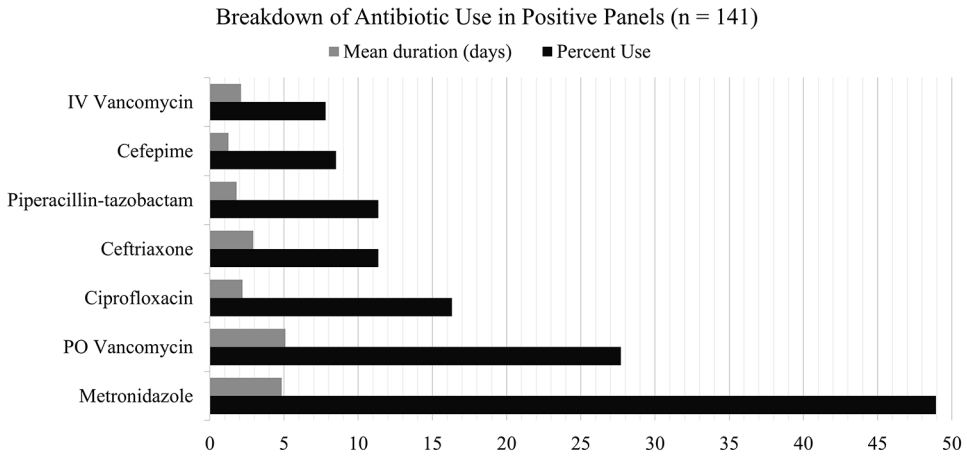


**Figure 5.** Breakdown of antibiotic use in positive panels. The most commonly used agents in this population were metronidazole (48.9%), oral vancomycin (27.7%), and ciprofloxacin (16.3%).

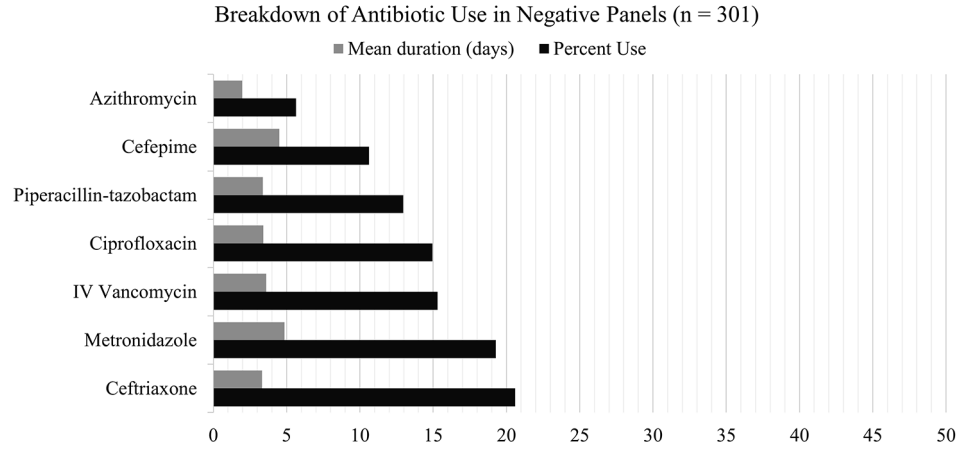


**Figure 6.** Breakdown of antibiotic use in negative panels. The most commonly used agents in this population were ceftriaxone (20.6%), metronidazole (19.3%), and intravenous vancomycin (16.3%).

common agents used in patients with negative GI panels were ceftriaxone (20.6%), metronidazole (19.3%), and intravenous vancomycin (16.3%).

Antibiotic therapy duration was also compared between panels with either a negative or a viral result ($n = 288$) and panels with a bacterial result ($n = 92$). Altogether, these patients received an average of 2.6 days and 5.0 days of antibiotics, respectively ($p < 0.001$), and additional culture positivity rates were not significantly different between groups (37.3% *versus* 32.9%, $p = 0.503$). In the cohort with negative or viral panel results, 114/288 (39.6%) did not receive antibiotic therapy, compared with 14/92 (15.2%) in the bacteria positive cohort ($p < 0.0001$). When excluding those who did not receive antibiotics, average days of therapy was 4.3 days for negative or viral positive panels and 5.9 days for bacteria positive panels.

### *Impact on other microbiological studies*

Looking at traditional non-PCR technology, there were 344 encounters with the GI panel that also had culture data and 70 encounters that had an ova and parasite (O&P) exam. The most common culture site was blood (65.4%), followed by urine (50%), stool (44.5%), and respiratory (14.8%). Overall, additional cultures were positive in 40.4%

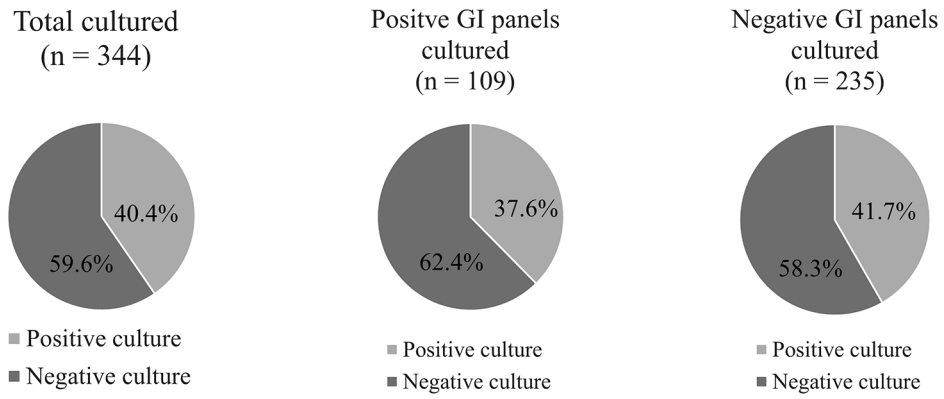


**Figure 7.** Culture positivity by GI panel result. In 344 cases, a culture was taken in addition to the GI panel. Overall, 40.4% of these additional cultures were positive.
GI panel, BioFire® Gastrointestinal panel.

of cases; Figure 7 displays culture positivity by GI panel result. All O&P exams performed were negative.

## Discussion

In one of the largest reports of the BioFire FilmArray® GI panel to date, we assessed 442 uses of the GI panel over a nearly 3-year period, and found a 31.9% positivity rate, similar to previously reported data.[5,8] The most commonly identified pathogen by the GI panel was *C. difficile*, a leading cause of both community-acquired and nosocomial infectious diarrhea.[3,4,9] Investigators determined "inappropriate use" criteria based on factors considered wasteful (i.e., duplicate testing with *C. difficile* PCR, performed after 48 h of hospitalization or no documented evidence of diarrhea) or confounding factors for interpretation of results (e.g., laxative use). There were 118 records that had duplicate *C. difficile* testing with the singleplex *C. difficile* PCR, a distinct opportunity for diagnostic stewardship intervention. The majority of redundant testing (73.7%) was done on the same stool sample. Interdepartmental education on appropriateness of testing is valuable, but many institutions have leveraged the EHR to implement a "soft" or "hard" stop, blocking duplicate ordering of these tests on an individual patient.[10] In addition, tests performed after 48 h of hospitalization which detect *C. difficile* may result in the CDI labeled as hospital-acquired, despite a community-onset of infection, impacting infection control metrics and potentially reimbursement.[11] The GI multiplex panel has a 98.5% sensitivity to *C. difficile* toxin A/B, making it difficult to distinguish between colonization and infection with panel results alone.[2] Of note, we determined a 1.7% discordance rate as there were two instances where the GI panel detected *C. difficile* and the Xpert® did not. This could be due to stool sample quality or difference in gene detection by these tests.[12] There were no instances where the Xpert® was positive and the GI panel was negative.

There are numerous reasons, both infections and non-infectious, for acute or chronic diarrhea that interfere with interpretation of results and appropriateness of testing. Laxative use in the preceding 48 h could potentially account for diarrhea or loose stools. Laxative use was included in our inappropriate use definition and was common among all patients (8%). Stool softener use was assessed (10% among all patients) but not included in our definition of inappropriate due to inconclusive evidence on effectiveness.[13] Significant changes in nutritional delivery, including enteral tube feeds, prompted by gastrointestinal disease or surgery, can be associated with both acute and sustained diarrhea.[14] Tube feed use was significantly more common in patients with a negative GI PCR panel (8.3% *versus* 1.4%) but was not included in the definition of inappropriate test for this study. The use of tube feeds and laxatives should be considered a criteria in the future for diagnostic stewardship of the GI panel as a potential non-infectious cause of diarrhea. Similarly, diarrhea should be present in the review of symptoms and documented before any tests should be conducted. As mentioned previously, leveraging the EHR to

implement a "stop" to ordering the GI panel for firm or solid stool samples should be considered.[10] Among the 268 records that met "inappropriate" use criteria, 43% ($n=116$) were performed greater than 2 days following initial hospitalization. Our definition of inappropriate use included panels run after more than 48 h of hospital admission due to the low likelihood of these pathogens being community-acquired and the aforementioned concerns with CDI. Baghdadi and colleagues showed diminished utility and lack of novel diagnoses when a multiplex GI panel was run after more than 72 h of hospitalization.[15] Panels conducted well into hospital admission are not useful, and increase the risk of incidental or collateral findings. Concerns with hospital-acquired CDI should prompt testing with a *C. difficile*-specific test. Negative GI panel results were more common across all inappropriate use criteria, significantly so in those without documented diarrhea ($p=0.009$), so wasteful testing could be mitigated through diagnostic stewardship education and leveraging the EHR to guide clinicians to appropriate use of the GI PCR panel.

The utility of multiplex GI panels in antimicrobial stewardship initiatives has been well studied. These tests have recently been shown to reduce time to appropriate antibiotic therapy and reduce length of stay when compared with conventional methods.[16] They also provide a cost benefit *via* reducing additional diagnostic stool tests and imaging studies.[5] Generally, the results of the GI panel in this study produced an observable difference in antibiotic therapy as those with negative panel results had reduced exposure to antibiotics. Of the patients with negative GI panels, 113/301 (37.5%) did not receive antibiotics while inpatient, and, in those that did receive antibiotic therapy, the duration was numerically shorter (5.4 days *versus* 4.8 days). When looking at the positive GI panel cohort, the high use of metronidazole and oral vancomycin, aligns with the high proportion of *C. difficile* toxin A/B identified in this group. As expected, positive panel results aided in achieving targeted antibiotic therapy. However, when looking at the 288 encounters where the panel did not indicate antibiotics (negative or viral results) there were 174 cases where at least one antibiotic was given (60.4%). Of those cases, 144 had separate cultures drawn, predominantly blood (74.5%) and urine (57.9%). These cultures were positive in 67/144 (46.5%) instances, leaving 77/144 (53.5%) to receive antibiotics potentially not indicated by culture data or panel results. In the group where culture data indicated antibiotics and the GI panel did not, 43/67 (64.2%) met inappropriate use criteria. In these patients, with more stringent screening, unnecessary use of multiplex GI panels could be markedly reduced. Therefore, the best way to optimize patient care is both further integration of antibiotic stewardship for those who received antibiotics without indication, and implementing diagnostic stewardship measures for those where GI panel results were less relevant to the nidus of infection.

Many clinicians and staff across numerous departments are responsible for the ordering, conducting, and interpretation of these tests. The large proportion of inappropriate tests in this study indicate the need for enhanced diagnostic stewardship. Using electronic means, such as leveraging the EHR, appears to be effective in implementing stewardship principles into diagnostics of acute diarrhea. These results will prompt the implementation of both "soft" and "hard" stop criteria into the EHR for the GI PCR panel. Restrictions on timing of test ordering relative to hospital admission and repeat testing will be included. Reducing redundancy in microbiologic tests will be a focus and included in the EHR "hard" stops. Given the dynamic and advancing landscape of rapid diagnostics, continued clinician education by stewardship teams will help ensure appropriate interpretation and optimal antimicrobial use based on testing results. All clinicians have a responsibility to be stewards of the available diagnostics and antimicrobials to improve cost effective patient care.

## Author contributions

PBB conceived and designed the analysis. MO and HM collected the data. MO performed the analysis and designed the figures. MO and PBB wrote the paper in consultation with HM, SD, MA, and JJ. All authors discussed the results and commented on the manuscript.

## Conflict of interest statement

Julie Ann Justo: bioMérieux Speaker's Bureau (non-branded content). P. Brandon Bookstaver: bioMérieux Speaker's Bureau (non-branded content). All other authors have no conflicts of interest.

## Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

## ORCID iDs

Melissa O'Neal https://orcid.org/0000-0003-0979-5463

Sangita Dash https://orcid.org/0000-0002-3986-0062


## References


1. Garibyan L and Avashia N. Polymerase chain reaction. *J Invest Dermatol* 2013; 133: 1–4.
2. The BioFire® FilmArray® Gastrointestinal (GI) Panel. *BioFire Diagnostics, LLC*, https://www.biofiredx.com/products/the-filmarray-panels/filmarraygi/ (2019, accessed October 14, 2019).
3. Younas M, Royer J, Weissman SB, *et al.* Burden of community-associated ***Clostridioides difficile*** infection in southeastern United States: a population-based study. *Infection* 2020; 48: 129–132.
4. Guh AY, Mu Y, Winston LG, *et al.* Trends in U.S. Burden of ***Clostridioides difficile*** Infection and Outcomes. *N Engl J Med* 2020; 382: 1320–1330.
5. Beal SG, Tremblay EE, Toffel S, *et al.* A gastrointestinal PCR panel improves clinical management and lowers health care costs. *J Clin Microbiol* 2017; 56: 1–9.
6. Al-Hasan MN, Winders HR, Bookstaver PB, *et al.* Direct measurement of performance: a new era in antimicrobial Stewardship. *Antibiotics (Basel)* 2019; 8: 1–19.
7. Foster RA, Madison B, Kuper K, *et al.* Pharmacists' familiarity with and institutional utilization of rapid diagnostic technologies for antimicrobial Stewardship. *Infect Control Hosp Epidemiol* 2017; 38: 863–866.
8. Khare R, Espy MJ, Cebelinski E, *et al.* Comparative evaluation of two commercial multiplex panels for detection of gastrointestinal pathogens by use of clinical stool specimens. *J Clin Microbiol* 2014; 52: 3667–3673.
9. Hodges K and Gill R. Infectious diarrhea: cellular and molecular mechanisms. *Gut Microbes* 2010; 1: 4–21.
10. Marcelin JR, Brewer C, Beachy M, *et al.* Hardwiring diagnostic stewardship using electronic ordering restrictions for gastrointestinal pathogen testing. *Infect Control Hosp Epidemiol* 2019; 40: 668–673.
11. Kotila SM, Mentula S, Ollgren J, *et al.* Community- and healthcare-associated Clostridium difficile infections, Finland, 2008−2013. *Emerg Infect Dis* 2016; 22: 1747–1753.
12. Martínez-Meléndez A, Camacho-Ortiz A, Morfin-Otero R, *et al.* Current knowledge on the laboratory diagnosis of Clostridium difficile infection. *World J Gastroenterol* 2017; 23: 1552–1567.
13. Tarumi Y, Wilson MP, Szafran O, *et al.* Randomized, double-blind, placebo-controlled trial of oral docusate in the management of constipation in hospice patients. *J Pain Symptom Manage* 2013; 45: 2–13.
14. Bowling TE. Diarrhoea in the enterally fed patient. *Frontline Gastroenterol* 2010; 1: 140–143.
15. Baghdadi JD, Coffey KC, Leekha S, *et al.* Diagnostic Stewardship for comprehensive gastrointestinal pathogen panel tests. *Curr Infect Dis Rep* 2020; 22.
16. Torres-Miranda D, Akselrod H, Karsner R, *et al.* Use of BioFire FilmArray gastrointestinal PCR panel associated with reductions in antibiotic use, time to optimal antibiotics, and length of stay. *BMC Gastroenterol* 2020; 20: 246.