Using Molecular GI Testing to Improve Laboratory Efficiency and Patient Management

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Disclosure

- Consultant: ThermoFisher Scientific, bioMérieux, BD
- Research: bioMérieux, Luminex, Hologic

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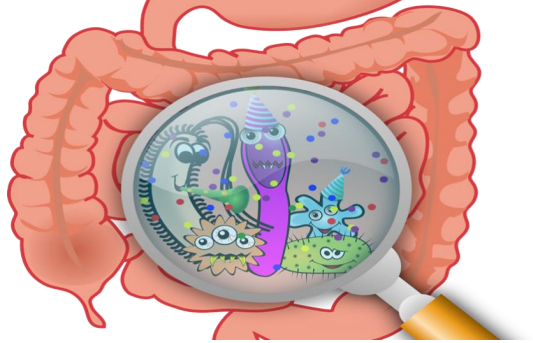
Objectives

- Summarize the etiology of gastrointestinal infections
- Summarize the current approaches to diagnosing gastrointestinal infections
- Discuss the role of molecular GI testing in patient management

Gastroenteritis



Acute gastroenteritis (AGE) remains a leading cause of morbidity and mortality worldwide

Substantial driver of annual healthcare services:

- 73 million outpatient encounters
- 1.8 million hospitalization
- 3,100 deaths
- $6 billion in medical care and lost productivity

WHO describes impact of 33 million disability-adjusted life years

- Children <5 y represents 40% of burden

~80% of AGE are unattributed

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Clin Infect Dis, Volume 32, Issue 3, 1 February 2001, Pages 331–351, https://doi.org/10.1086/318514

Epidemiology and Economic Burden of Acute Infectious Gastroenteritis Among Adults Treated in Outpatient Settings in US Health Systems

Moon, Rena C. MD, MPH[1]; Bleak, Tammy C. PharmD, MSc[2]; Rosenthal, Ning A. PhD, MD, MPH[1]; Couturier, Brianne PhD[2]; Hemmert, Rachael MSPH[2]; Timbrook, Tristan T. PharmD, MBA[2]; Brown, Harold MHA, MBA[1]; Fang, Ferric C. MD[3]

Author Information

The American Journal of Gastroenterology 118(6):p 1069-1079, June 2023. | **DOI:** 10.14309/ajg.0000000000002186

- Among 248,896 patients, 62% had no preexisting conditions
- 84.7% presented to the ED and 96.4% were discharged
- Within 30 days of discharge, 1% were hospitalized and 2.8% had another outpatient visit due to AGE
- Mean cost per patient was $1,338 = $333,060,182

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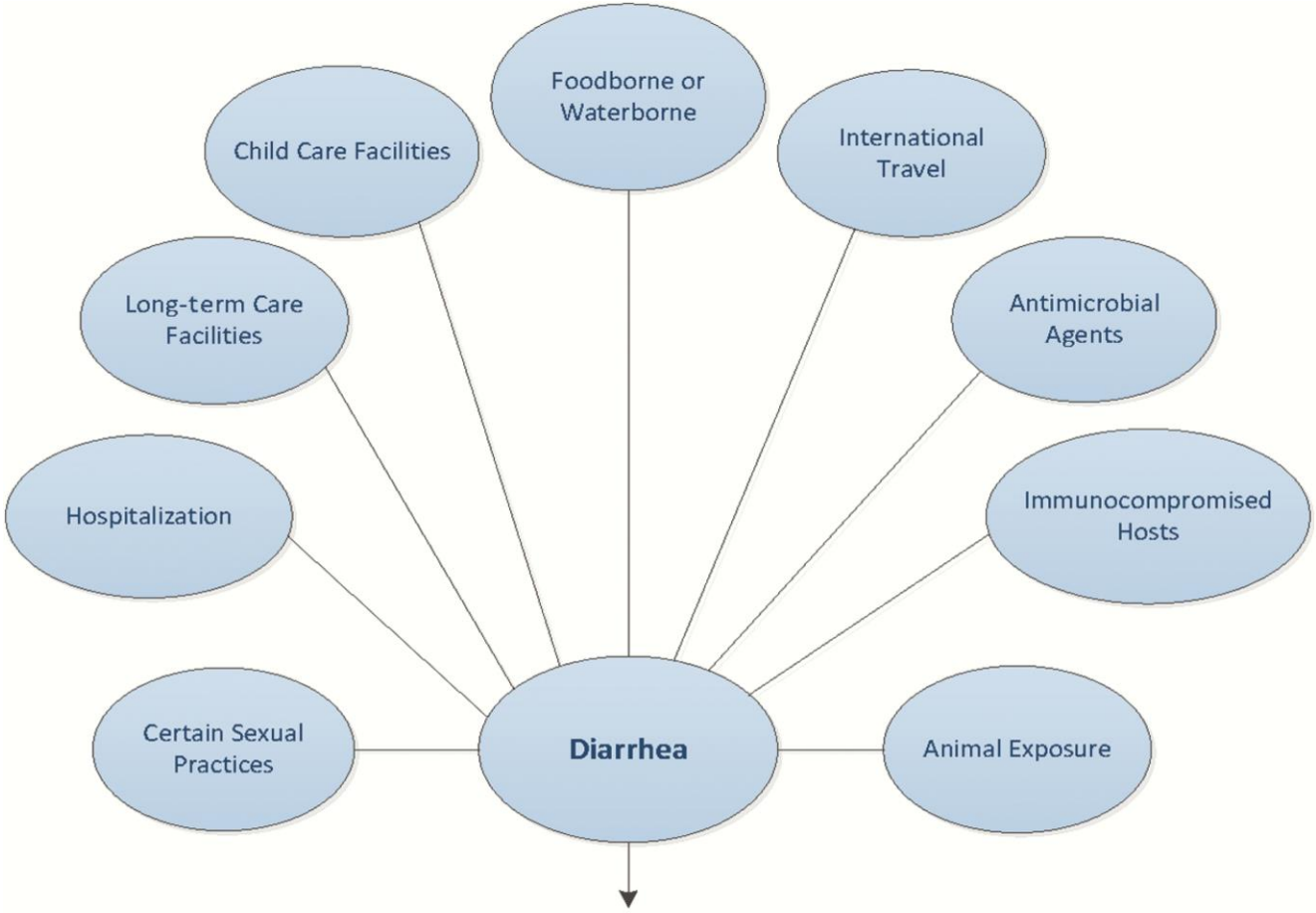
Considerations when evaluating for infectious diarrhea



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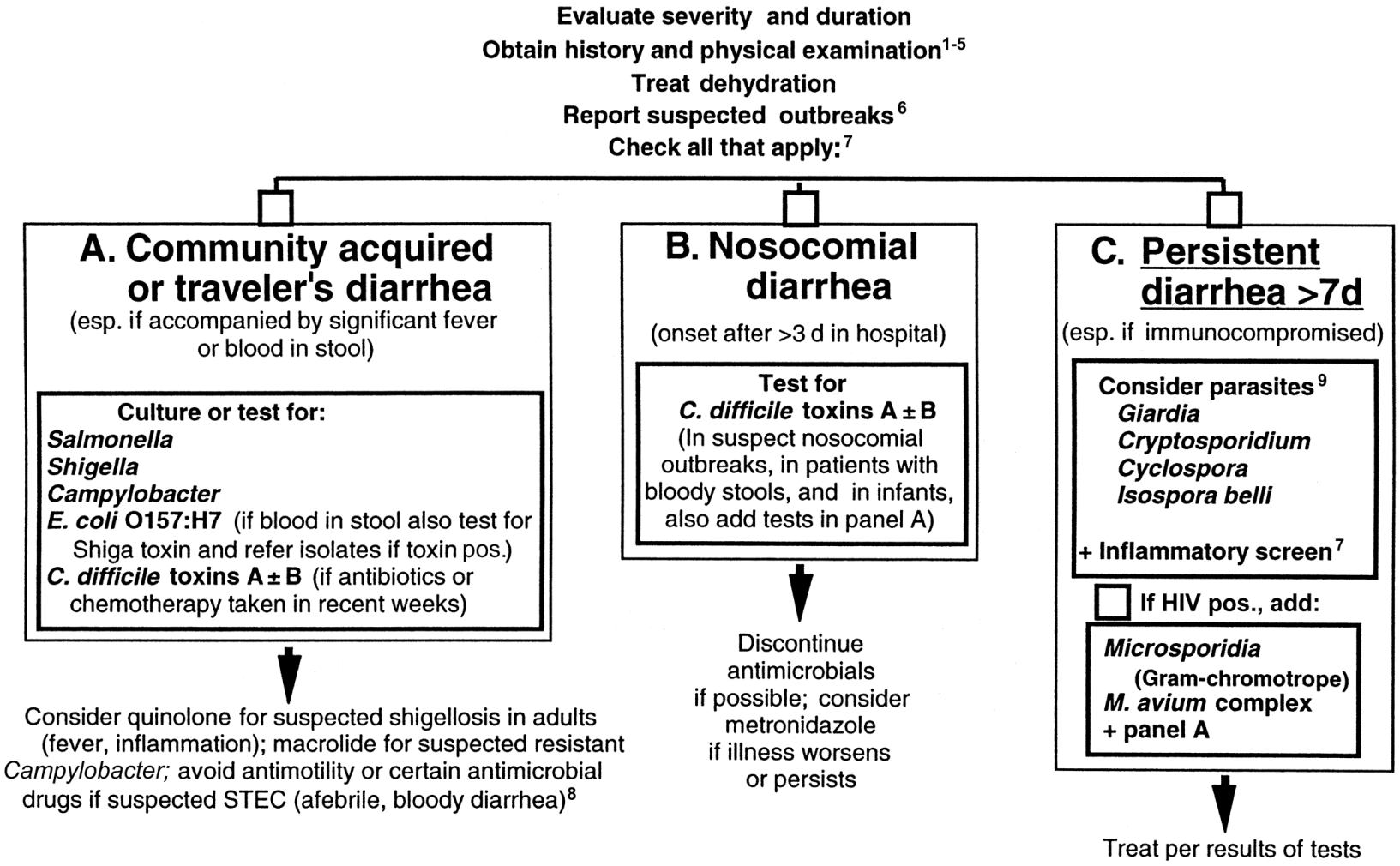
Clin Infect Dis, Volume 65, Issue 12, 15 December 2017, Pages e45–e80, https://doi.org/10.1093/cid/cix669

Recommendations for the diagnosis and management of diarrheal illnesses



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Clin Infect Dis, Volume 32, Issue 3, 1 February 2001, Pages 331–351, https://doi.org/10.1086/318514

Clinical Presentations Suggestive of Infectious Diarrhea Etiologies

Finding	Likely Pathogens
Persistent or chronic diarrhea	*Cryptosporidium* spp, *Giardia lamblia*, *Cyclospora cayetanensis*, *Cystoisospora belli*, and *Entamoeba histolytica*
Visible blood in stool	STEC, *Shigella, Salmonella, Campylobacter, Entamoeba histolytica, noncholera Vibrio species, Yersinia, Balantidium coli, Plesiomonas*
Fever	Not highly discriminatory—viral, bacterial, and parasitic infections can cause fever. In general, higher temperatures are suggestive of bacterial etiology or *E. histolytica*. Patients infected with STEC usually are not febrile at time of presentation
Abdominal pain	STEC, *Salmonella, Shigella, Campylobacter, Yersinia,* noncholera *Vibrio* species, *Clostridium difficile*
Severe abdominal pain, often grossly bloody stools (occasionally nonbloody), and minimal or no fever	STEC, *Salmonella, Shigella, Campylobacter,* and *Yersinia enterocolitica*
Persistent abdominal pain and fever	*Y. enterocolitica* and *Y. pseudotuberculosis*; may mimic appendicitis
Nausea and vomiting lasting ≤24 hours	Ingestion of *Staphylococcus aureus* enterotoxin or *Bacillus cereus* (short-incubation emetic syndrome)
Diarrhea and abdominal cramping lasting 1–2 days	Ingestion of *Clostridium perfringens* or *B. cereus* (long-incubation emetic syndrome)
Vomiting and nonbloody diarrhea lasting 2–3 days or less	Norovirus (low-grade fever usually present during the first 24 hours in 40% if infections)
Chronic watery diarrhea, often lasting a year or more	Brainerd diarrhea (etiologic agent has not been identified); postinfectious irritable bowel syndrome

Clin Infect Dis, Volume 65, Issue 12, 15 December 2017, Pages e45–e80, https://doi.org/10.1093/cid/cix669

Table 3 All-listed causes of infectious enteritis in treat-and-release emergency department visits, 2010

Diagnosis (ICD-9-CM code)	Overall ranking	Rate of ED visits per 100,000, by age					Total number of ED visits
		<1	1–17	18–44	45–64	65+	
All infectious enteritis cases							**313,900**
Viral enteritis not otherwise specified (008.8)	1	424.6	137.6	74.3	28.4	31.1	233,200
Ill-defined intestinal infections (009.0–009.3)	2	33.9	12.0	16.6	10.0	8.7	40,100
Unspecified bacterial food poisoning (005.9)	3	1.1	5.1	11.5	6.1	5.3	23,700
Unspecified bacterial intestinal infection (008.5)	4	1.7	0.9	2.5	1.4	1.3	5,200
Hepatitis A (070.0–070.1)	5	0.2	0.1	0.9	2.0	0.9	3,100
Protozoal intestinal diseases (006.0–007.9)	6	0.3	0.6	0.6	0.3	0.4	1,600
Salmonella (003.0–003.9)	7	5.8	0.5	0.3	0.2	0.2	1,200
Other specific foodborne infections (023.0–023.9; 027.0; 124; 130.0–130.9)	8	0.0	0.1	0.6	0.4	0.2	1,200
Rotavirus enteritis (008.61)	9	6.2	1.2	0.0	0.0	0.0	1,100
Other specified viral enteritis (008.6; 008.62–008.69)	10	2.9	0.5	0.2	0.2	0.2	1,000
Campylobacter intestinal infection (008.43)	11	0.4	0.2	0.2	0.2	0.2	600
Other specified bacterial food poisoning (005.0–005.89)	12	0.0	0.0	0.2	0.2	0.1	500
E. coli enteritis (008.00–008.09)	13	0.3	0.2	0.1	0.1	0.2	400
Shigella (004.0–004.9)	14	0.5	0.3	0.1	0.0	0.0	400
Other specified bacterial intestinal infections (008.1–008.42; 008.44; 008.46–008.49)	15	0.3	0.1	0.1	0.1	0.1	400
Cholera, typhoid, and paratyphoid (001.0–002.9)	16	0.1	0.1	0.1	0.1	0.1	300

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Current guidelines

- 2017 IDSA guideline recommends a variety of approaches including NAAT, culture, O&P

- "Molecular techniques generally are more sensitive and less dependent than culture on the quality of specimen."
- "Culture independent multiplex molecular tests are reported to be more sensitive than culture, result in higher rates of detection, and often cost more than culture methods."

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Miller et al. Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2024 Update by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM) , *Clinical Infectious Diseases*, 2024

Clin Infect Dis, Volume 65, Issue 12, 15 December 2017, Pages e45–e80, https://doi.org/10.1093/cid/cix669

Inconsistent criteria

Table 1. Case Characteristics and Symptoms Referenced in Acute Gastroenteritis Guidelines, Algorithms, and Published Reports

	CDC [12]	Klein et al[a] [24]	NICE[b] [4]	Hatchette and Farina [13]	ESPGHAN [14]	IDSA [15]
Applies to	Children with ≥3 diarrhea events in 24 hours	Children and young adults with diarrhea	Children <5yo with ≤14 days diarrhea	Children and adults with ≥1 day diarrhea	Children with decrease in stool consistency and/or increase in frequency	Children and adults with diarrhea
Recent antibiotics use	-	absent	-	-	-	-
International travel	-	history	recent history	-	history	recent history if diarrhea lasts ≥14 days
Daycare attendance[c]	-	-	-	present	-	-
Underlying chronic condition[d]	-	-	-	present	present	-
Diarrhea events in 24 hours	-	>10	-	-	>10[e]	-
Diarrhea duration	-	≤10 days	≥7	-	>14 days[f]	-
Vomiting events in 24 hours	-	<1	-	-	-	-
Blood in stool	present	present	present	present	present	present
Fever	-	present	-	present	-	present
Dehydration score	-	-	-	present	(severe)[e]	-
Maximal pain level	-	-	-	-	-	(severe)
Other criteria[g]	X	-	X	X	X	X

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Tarr GAM, et al. Clin Infect Dis. 2019 Sep 13;69(7):1173-1182. doi: 10.1093/cid/ciy1021.

Inconsistent stool testing recommendation

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Blood in stool	present	present	present	present	present	present
Fever	-	present	-	present	-	present
Dehydration score	-	-	-	present	(severe)[e]	-
Maximal pain level	-	-	-	-	-	(severe)
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Table 2. Pathogen Detection by Symptom Complex at Index Presentation and at the Completion of 14-Day Follow-up

		Symptom Complex Index Presentation n (%)			Symptom Complex 14-Day Follow-up n (%)		
Pathogen	Total Cases[a]	Isolated Diarrhea	Diarrhea + Vomiting	Isolated Vomiting	Isolated Diarrhea	Diarrhea + Vomiting	Isolated Vomiting
Bacteria	144	59 (41.0)	49 (34.0)	36 (25.0)	55 (38.2)	64 (44.4)	25 (17.4)
Salmonella spp.	54	32 (59)	12 (22)	10 (19)	29 (54)	18 (33)	7 (13)
Aeromonas spp.	26	5 (19)	11 (42)	10 (38)	4 (15)	14 (54)	8 (31)
Campylobacter spp.	18	8 (44)	8 (44)	2 (11)	8 (44)	9 (50)	1 (6)
STEC, non-O157	17	4 (24)	8 (47)	5 (29)	4 (24)	9 (53)	4 (24)
Escherichia coli O157	10	4 (40)	3 (30)	3 (30)[b]	4 (40)	5 (50)	1 (10)
Shigella spp.	8	3 (38)	4 (50)	1 (13)	3 (38)	4 (50)	1 (13)
ETEC	6	2 (33)	2 (33)	2 (33)	2 (33)	4 (67)	0 (0)
Yersinia spp.	5	1 (20)	1 (20)	3 (60)	1 (20)	1 (20)	3 (60)
Vibrio spp.	0	-	-	-	-	-	-
Clostridioides difficile[c]	46	4 (9)	11 (24)	31 (67)	4 (9)	20 (43)	22 (48)
Virus(es)	1520	212 (13.9)	585 (38.5)	723 (47.6)	188 (12.4)	893 (58.8)	439 (28.9)
Parasite(s)	11	1 (9)	5 (45)	5 (45)	0 (0)	7 (64)	4 (36)
No pathogen detected	769	153 (19.9)	135 (17.6)	481 (62.5)	147 (19.1)	234 (30.4)	388 (50.5)

Symptom complex refers to the combination of ≥3 diarrhea episodes or ≥3 vomiting episodes in a 24-hour period, necessary to meet the definition of acute gastroenteritis.

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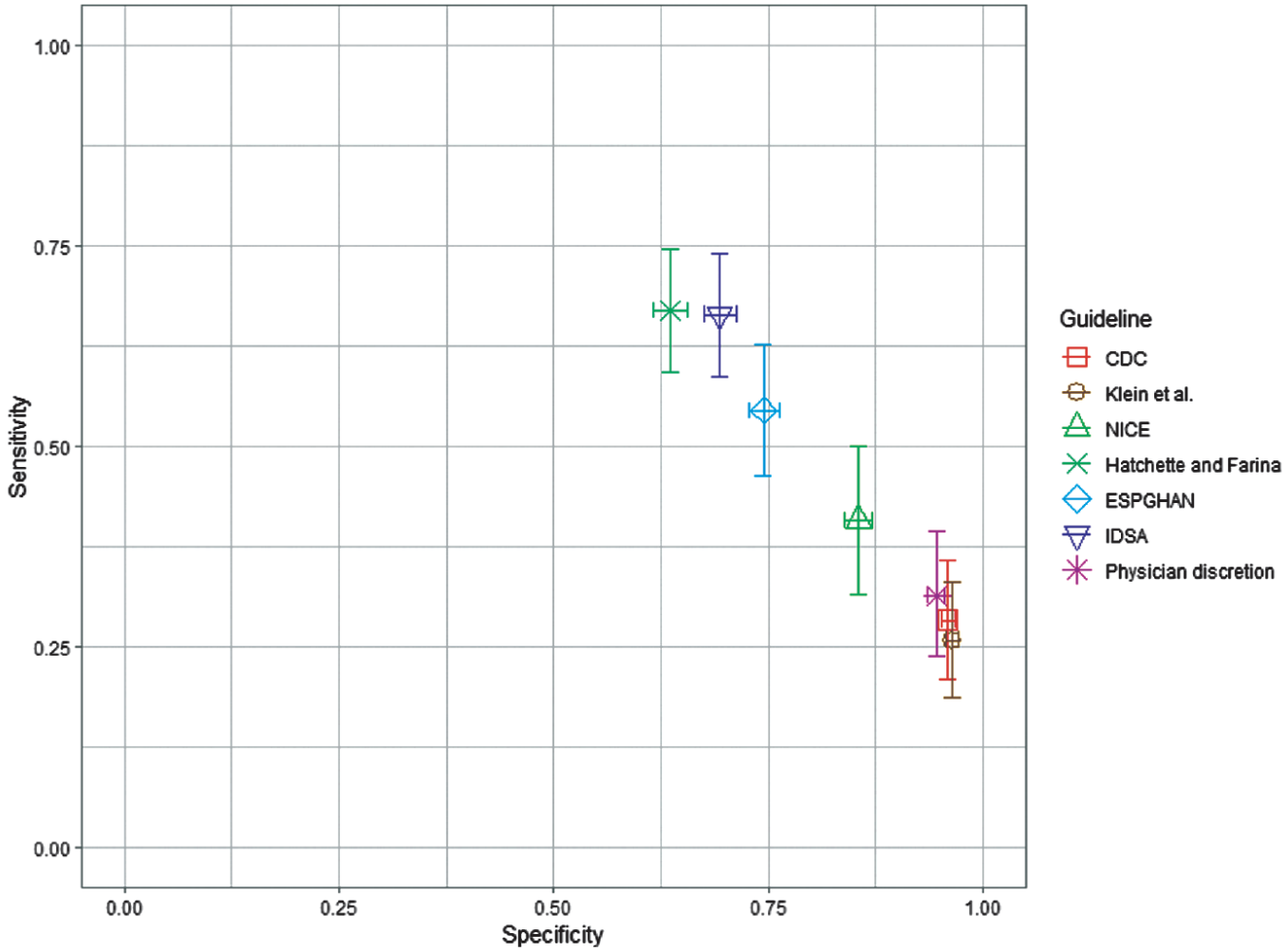

- Guideline sensitivity ranged from 25.8% to 66.9%
- Guideline specificity ranged from 63.6% to 96.5%
- The most sensitive guidelines missed 1/3 of cases
- The most specific guidelines missed almost 75% of cases

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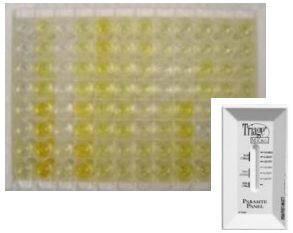
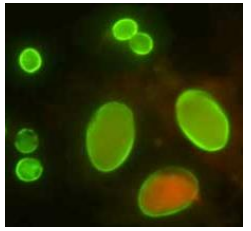
Why Molecular GI Panels?

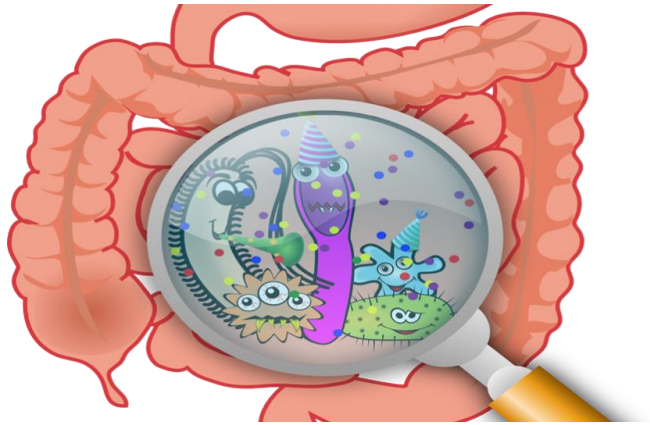
- Broad spectrum of pathogens present with similar signs and symptoms
- Increased detection of pathogens
- Polymicrobial infections
  - Increase detection
  - Optimize therapy
- Conventional work up can be multi-factorial and complicated
- Faster turn-around-time

Limitations associated with current testing methods



- Time-consuming
- Labor-intensive
- Technically complex methods



- Limited coverage
- Lower sensitivity and specificity
- Overlapping symptoms

- High cost with minimum benefit
- Slow TAT

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Potential Benefits of a GI Panel

- Allows for comprehensive, rapid diagnosis of infectious gastroenteritis
  - Address issue of clinicians not knowing what's included in traditional methods
- Most clinicians do not order laboratory work up of diarrhea
  - [1]Only 21% of stool studies ordered on patients presenting with gastroenteritis
    - 89% of these patients submitted specimen for testing
- Change clinician's practice if a faster more sensitive test is available?

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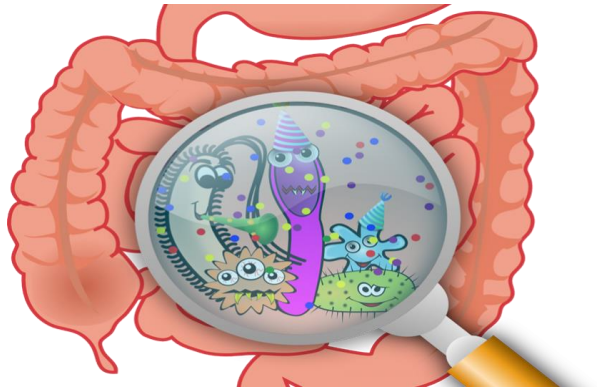
Herikstad H, et al. Epidemiol. Infect. 2002;129:9-17

Benefits

- Faster time to result
- Higher detection rate
- Streamlined order
- Streamlined testing
- Improved infection prevention
- Decreased antibiotic use
- Decreased isolation days
- Decreased hospital costs
- Decreased patient costs



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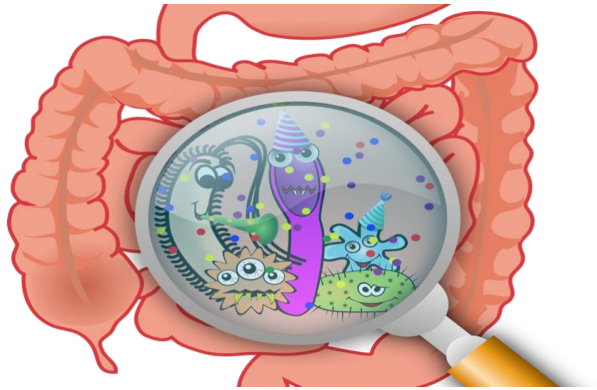
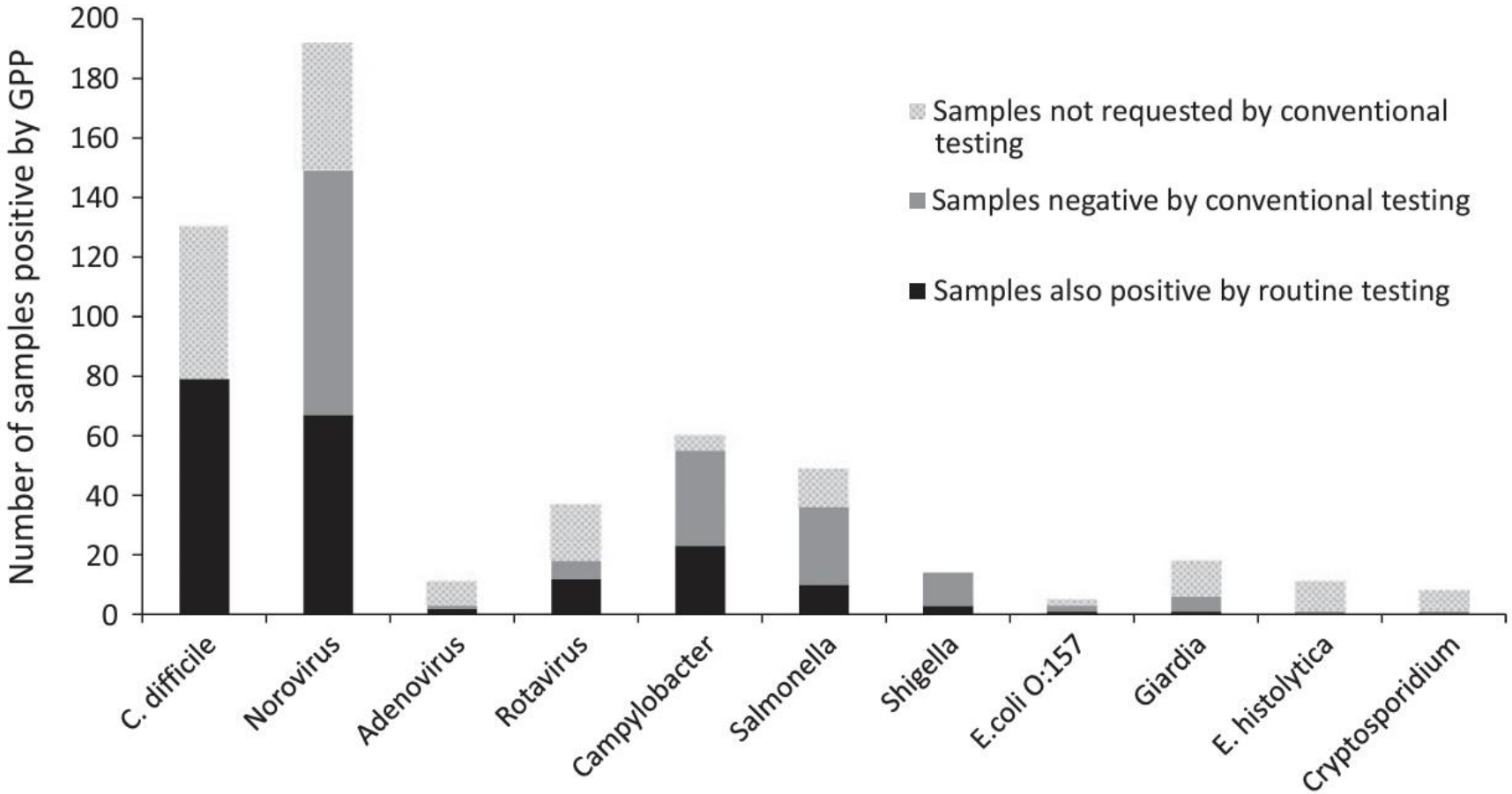


Limitations

- Increased lab costs
- Decreased reimbursement

Improved pathogen detection



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Halligan E, Clin Microbiol Infect. 2014 Aug;20(8):O460-7.

Improved pathogen detection

Patients and pathogens	GI PCR (N = 9,402)	Stool culture, O&P, and Rotavirus/adenovirus EIA (N = 5,986)	P value
Patients with a pathogen	2,746 (29.2)	246 (4.1)	
Pathogens identified	3,804	251	
Viruses	1,073 (39.1)	38/246 (15.4)	0.001
Bacteria	1,792 (65.3)	202/246 (82.1)	0.001
Parasite	226 (8.2)	9/246 (3.7)	0.011

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Axelrad et al. J Clin Microbiol 57:10.1128/jcm.01775-18.https://doi.org/10.1128/jcm.01775-18

Avoidance of procedure and antibiotics

Variable	GI PCR (N = 9,402)	Culture (N = 5,986)	P value
Endoscopy within 30 days			
No procedures	8,615 (91.6)	5,410 (90.4)	0.008
Any procedure	787 (8.4)	576 (9.6)	0.008
Emergency department visit within 30 days	1,158 (12.3)	789 (13.2)	0.116
Radiology within 30 days			
Any abdominal radiology	2,760 (29.4)	1,897 (31.7)	0.002
Antibiotics within 14 days			
Any antibiotic	3,408 (36.2)	2,449 (40.9)	0.001
Length of stay from test to discharge			
Median (IQR)	5 (2–13)	5 (2–13)	
Mean (SD)	12.4 (21.9)	11.8 (20.0)	0.087

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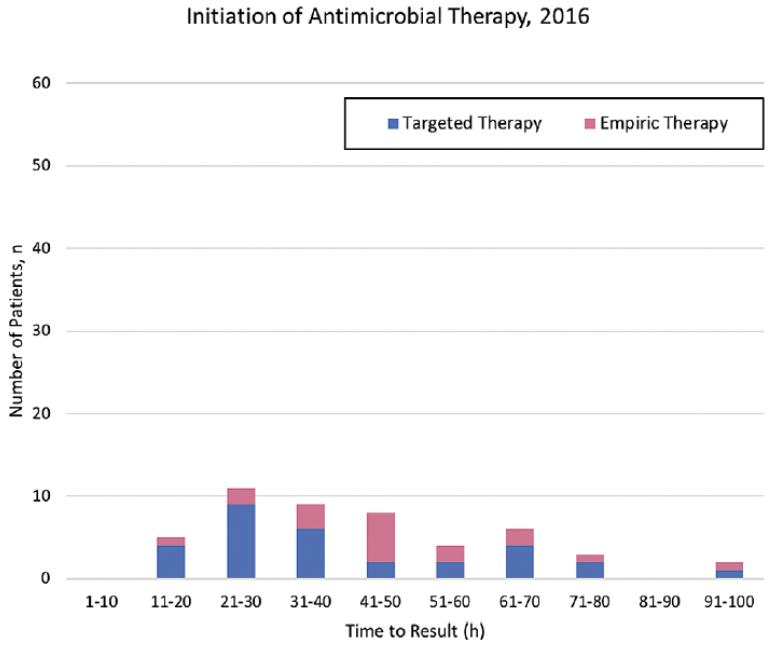
Axelrad et al. J Clin Microbiol 57:10.1128/jcm.01775-18.https://doi.org/10.1128/jcm.01775-18

Improved time to targeted therapy



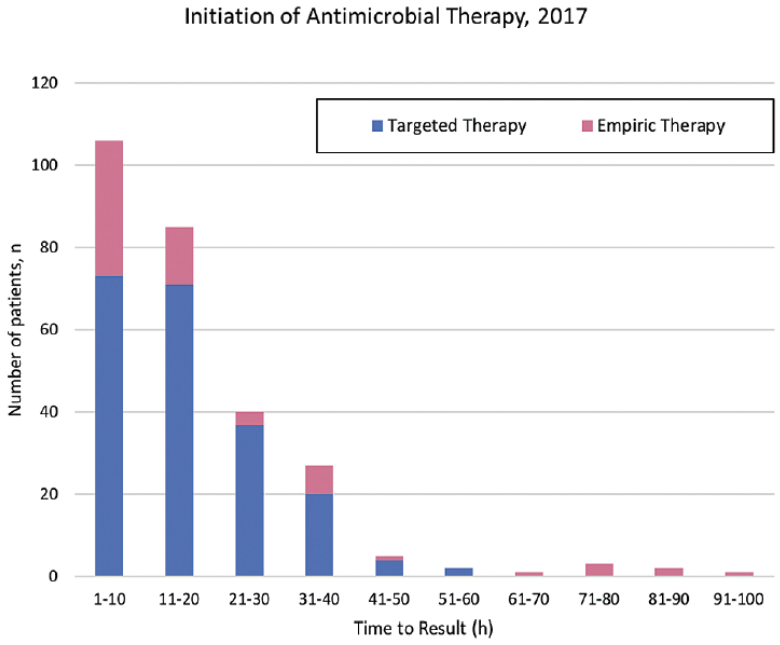


Table 1. Comparison of FilmArray™ and Stool Culture Turnaround Times and Impact on Clinical Decisions

	2016 Culture	2017 FilmArray	*P* Value
Cases Reviewed, n	83	496	n/a
Median Time Collection to First Report (hours)	47.0	18.0	<.0001
Patients with bacteria/parasite identified, n	83	420	n/a
Eligible patients prescribed antimicrobials, n (%)	50 (60.3)	272 (63.8)	n.s.
Empirical antimicrobial prescription, n (%)	20 (40.0)	64 (23.5)	.0148
Median Time Collection to Antimicrobial (hours)	72.0	26.0	<.0001

Categorical values analyzed for statistical significance by Chi squared test. Comparison of medians performed with Mann-Whitney test.

Abbreviations: n/a, not applicable; n.s., not significant.

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Cybulski RJ Jr, et al. Clin Infect Dis. 2018 Nov 13;67(11):1688-1696.

Improved infection prevention and control practices

Table 1
Distribution of pathogens detected by the FilmArray GI Panel in diarrheal stool specimens that were negative for *C. difficile* and/or rotavirus by conventional testing.

Pathogen on FilmArray GI Panel	Number of samples testing positive for indicated analyte on the FilmArray GI panel that were originally negative or not tested for:		
	C. difficile, N = 142	Rotavirus[a], N = 16	All negative patients, N = 158
Norovirus	9 (2)[b]	1	10
Rotavirus	8 (2)		8
EPEC	8 (3)		8
EIEC/*Shigella*	2 (2)	1	3
EAEC	2		2
ETEC	2 (1)		2
Astrovirus		2 (1)	2
Salmonella		1	1
Cryptosporidium	1		1
Aeromonas	1		1
C. difficile	2	1 (1)	3
Adenovirus		1	1
Total pathogens	35/142 (24.6%)	7/16 (43.8%)	42/158 (26.6%)
Total patients	29/142 (20.4%)	6/16 (37.5%)	35/158 (22.2%)

[a] Includes 5 patients negative for both *C. difficile* and rotavirus.
[b] Numbers in parentheses indicate the number detected in specimens positive for more than 1 agent.

- 158 inpatient diarrheal stool specimens with molecular GI Panel that had been stored at −70°C after testing negative by conventional methods for *C. difficile* and/or rotavirus
- 22.2% had at least 1 other infectious agent detected, and 60% of patients were never placed in appropriate isolation for a total of 109 patient days
- 20.3% of patients with negative GI panel results could have been removed from isolation
  - 181 patient days of potentially unnecessary isolation

Rand KH et al. Diagn Microbiol Infect Dis. 2015 Jun;82(2):154-7. c

Table 3. Economic analysis of conventional and GPP testing pathways.

Conventional testing pathway	
Total number of isolation days	2202
Total isolation costs	£194,723
Total laboratory testing costs	£33,960
Total costs	£228,683
GPP testing pathway	
Total number of isolation days	1447
Total isolation costs	£127,958
Total GPP laboratory testing costs	£55,104
Total confirmatory testing costs[a]	£1139
Total laboratory testing costs	£56,243
Total costs	£184,201
Difference (GPP testing pathway – conventional testing pathway)	
Total number of isolation days	−755
Total isolation costs	−£66,765
Total laboratory testing costs	£22,283
Total costs	**£−44,482**

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Goldenberg SD et al. J Infect. 2015 May;70(5):504-11.

Decreased return ED visits

- Multicenter, prospective, pragmatic study between April 2015 and September 2016
  - 1157 patients (571 pre-intervention and 586 intervention)
- Higher proportion treatable pathogens detected during the pre-intervention (17.3%) period compared with clinician-ordered testing (3.2%) as well as clinically relevant pathogens (22% vs 2.8%).
- Potential pathogens were identified by clinician-ordered tests in 19 of 571 (3.3%) in the pre-intervention period compared with 434 of 586 (74%) in the intervention period
- The intervention was associated with a **21% reduction in the odds of any return visit** (odds ratio, 0.79; 95% confidence interval, .70–.90) after adjusting for potential confounders.
- Appropriate treatment was prescribed in 11.3% compared with 19.6% during the intervention period (P = .22).

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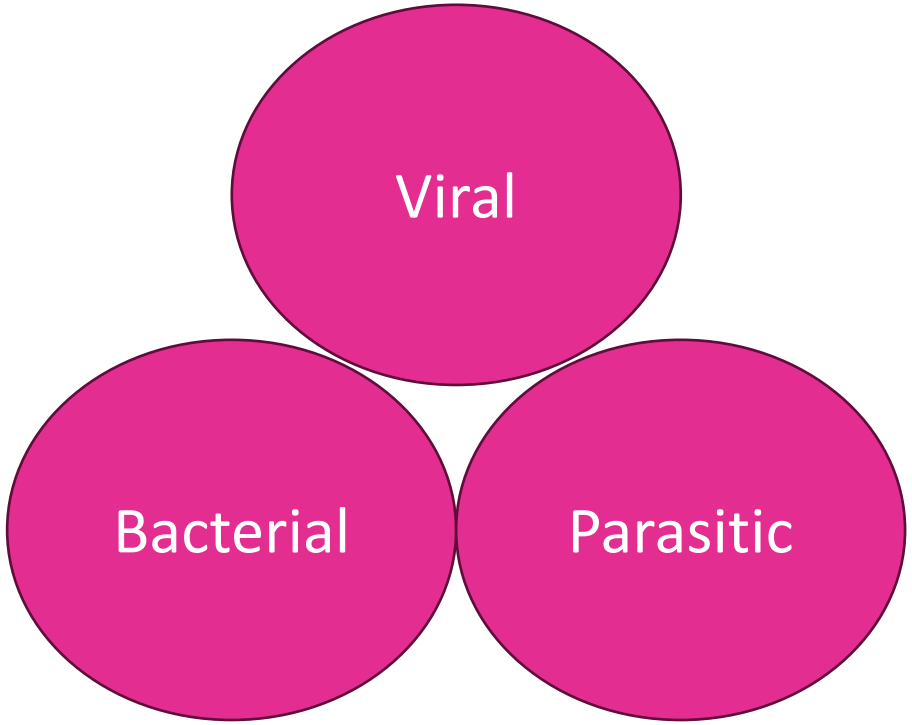
Pavia AT, et al. Clin Infect Dis. 2024 Mar 20;78(3):573-581.

Molecular testing options



VS

Large multiplexed panels (bacteria, viruses, parasites)

Target organism	BioFire Gastrointestinal Panel	Diasorin (Verigene) Enteric Pathogens Test	Luminex Gastrointestinal Pathogens Panel	BD BD MAX™	Hologic Prodesse ProGastro SSCS
Bacterial					
Campylobacter	X	X	X	X	X
Salmonella	X	X	X	X	X
Shigella	X	X	X	X	X
Shiga-like toxin 1/2 (STEC)	X	X[a]	X	X	X
Enterotoxigenic *E. coli*	X		X	*	
Enteropathogenic *E. coli*	X				
Enteroaggregative *E. coli*	X				
E. coli O157	X		X		
Vibrio	X	X		*	
Yersinia enterocolitica	X	X		*	
Plesiomonas shigelloides	X			*	
Clostridium difficile	X		X		
Viral					
Norovirus GI and GII	X	X	X	††	
Adenovirus 40/41	X		X	††	
Rotavirus	X	X	X	††	
Astrovirus	X			††	
Sapovirus	X			††	
Parasitic					
Giardia	X		X	+	
Cryptosporidium	X		X	+	
Cyclospora cayetanensis	X				
Entamoeba histolytica	X		X	+	

[a] Verigene detects and reports each shiga-like toxin gene separately

* BD MAX™ Extended Bacterial Panel

\+ BD MAX™ Enteric Parasite Panel

†† BD MAX™ Enteric Viral Panel

Target organism	BioFire Gastrointestinal Panel	Diasorin (Verigene) Enteric Pathogens Test	Luminex Gastrointestinal Pathogens Panel	BD BD MAX™	Hologic Prodesse ProGastro SSCS
Bacterial					
Campylobacter	X	X	X	X	X
Salmonella	X	X	X	X	X
Shigella	X	X	X	X	X
Shiga-like toxin 1/2 (STEC)	X	X[a]	X	X	X
Enterotoxigenic *E. coli*	X		X	*	
Enteropathogenic *E. coli*	X				
Enteroaggregative *E. coli*	X				
E. coli O157	X		X		
Vibrio	X	X		*	
Yersinia enterocolitica	X	X		*	
Plesiomonas shigelloides	X			*	
Clostridium difficile	X		X		
Viral					
Norovirus GI and GII	X	X	X	††	
Adenovirus 40/41	X		X	††	
Rotavirus	X	X	X	††	
Astrovirus	X			††	
Sapovirus	X			††	
Parasitic					
Giardia	X		X	+	
Cryptosporidium	X		X	+	
Cyclospora cayetanensis	X				
Entamoeba histolytica	X		X	+	

[a] Verigene detects and reports each shiga-like toxin gene separately

* **BD MAX™ Extended Bacterial Panel**

†† **BD MAX™ Enteric Viral Panel**

\+ **BD MAX™ Enteric Parasite Panel**

Table modified from Couturier MR & Dien Bard J. Clin Lab Med. 2019 Sep;39(3):433-451.

Analytical performances

Panel	Sensitivity	Specificity	Reference
BioFire GI Panel	94.5-100%	97.1-100%	Buss et al. JCM 2015
BD MAX™ xEBP	97.6-100%	99.7-99.9%	Simner et al. JCM 2017
Luminex GPP	95.8-100%	90.8-100%	Khare et al. JCM 2014
Verigene EP	71.4-95.4%	99.1-100%	Huang et al. DMID 2016

* Bacterial Culture, PCR, antigen test and microscopy

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Lewinski et al. J Mol Diagn. 2023 Dec;25(12):857-875.

Factors to consider when choosing a panel

Prevalence

Reimbursement

Clinical presentation

Cost/Budget

Targets

Lower prevalence of protozoal pathogens

- 1089 diarrheal episodes among 779 children
- 561 (52%) positive patients; 752 pathogens
- Norovirus was most common (11%)

Pathogen	Clinical Setting (n [%])		
	Outpatient (n = 285)	Emergency (n = 174)	Inpatient (n = 630)
Bacterial pathogens	75 (26.3)	49 (28.2)	166 (26.3)
Viral pathogens	62 (21.8)	78 (44.8)	146 (23.2)
Protozoal pathogens	18 (6.3)	9 (5.2)	9 (1.4)
Codetection	39 (13.7)	41 (23.6)	80 (12.7)
Negative	147 (51.6)	56 (32.2)	334 (53.0)

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Stockmann et al. J Ped Infect Dis 2016

Lower prevalence of protozoal pathogens

Pathogen	Total Cases[a]	Symptom Complex Index Presentation n (%)		
		Isolated Diarrhea	Diarrhea + Vomiting	Isolated Vomiting
Bacteria	144	59 (41.0)	49 (34.0)	36 (25.0)
Salmonella spp.	54	32 (59)	12 (22)	10 (19)
Aeromonas spp.	26	5 (19)	11 (42)	10 (38)
Campylobacter spp.	18	8 (44)	8 (44)	2 (11)
STEC, non-O157	17	4 (24)	8 (47)	5 (29)
Escherichia coli O157	10	4 (40)	3 (30)	3 (30)[b]
Shigella spp.	8	3 (38)	4 (50)	1 (13)
ETEC	6	2 (33)	2 (33)	2 (33)
Yersinia spp.	5	1 (20)	1 (20)	3 (60)
Vibrio spp.	0	-	-	-
Clostridioides difficile[c]	46	4 (9)	11 (24)	31 (67)
Virus(es)	1520	212 (13.9)	585 (38.5)	723 (47.6)
Parasite(s)	11	1 (9)	5 (45)	5 (45)
No pathogen detected	769	153 (19.9)	135 (17.6)	481 (62.5)

Table 3. Pathogens Detected by Clinician-Ordered Standard-of-Care Tests and by Multiplex Polymerase Chain Reaction by Study Period

Pathogen	Pre-Intervention		Intervention	
	Standard-of-Care Clinician-Ordered Tests (N = 571)	Multiplex PCR (N = 375), Clinician Blinded to Results	Standard-of-Care Clinician-Ordered Rests (N = 586)	Multiplex PCR (N = 586), Results Available to Clinician
Bacteria				
Campylobacter	4 (0.7%)	13 (3.5%)	1 (0.2%)	11 (1.9%)
Salmonella	2 (0.4%)	11 (2.9%)	6 (1.0%)	18 (3.1%)
Shigella/enteroinvasive E. coli	9 (1.6%)	33 (8.8%)	4 (0.8%)	24 (4.1%)[a]
Plesiomonas	…	0 (0)	…	2 (0.3%)
Yersinia	…	0 (0)	…	2 (0.3%)
Shigatoxin-producing *E. coli*	4 (0.7%)	14 (3.7%)	1 (0.2%)	14 (2.4%)
Escherichia coli O157	4 (0.7%)	3 (0.8%)	1 (0.2%)	3 (0.5%)
Enterotoxigenic *E. coli*	…	10 (2.7%)	…	6 (1.0%)
Enteroaggregative *E. coli*	…	21 (5.6%)	…	36 (6.1%)
Enteropathogenic *E. coli*	…	76 (20%)	…	67 (11.4%)
Clostridioides difficile	2 (0.4%)	43 (11.5%)	6 (0.6%)	94 (16.0%)[b]
C. difficile no virus and aged ≥2 y	1 (0.2%)	8 (2.1%)	1 (0.2%)	23 (3.9)
Viruses				
Adenovirus F 40/41	1 (0.2%)	33 (8.8%)	1 (0.2%)	61 (10.4%)
Astrovirus	…	6 (1.6%)	…	43 (7.3%)[a]
Norovirus GI/GII	…	57 (15.2%)	…	148 (25.3%)[a]
Rotavirus	2 (0.4%)	16 (4.3%)	1 (0.2%)	12 (2.0%)
Sapovirus	…	31 (8.3%)	…	66 (11.3%)
Any viral pathogen	3 (0.6%)	135 (36%)	2 (0.4%)	294 (50%)[a]
Protozoa	…	18 (3.1)	…	23 (3.9%)
Cryptosporidium	…	10 (2.7%)	…	14 (2.4%)
Cyclospora	…	0 (0)	…	0 (0)
Giardia	…	9 (2.4%)	…	9 (1.5%)
At least 1 potential pathogen	19 (3.3%)	262 (70%)	15 (3%)	434 (74%)
Any treatable pathogen[c]	14 (2.5%)	65 (17.3%)	5 (0.9%)	61 (10.4%)
Any clinically relevant pathogen[d]	16 (2.8%)	84 (22.4%)	12 (2%)	88 (15%)

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Tarr GAM, et al. Clin Infect Dis. 2019 Sep 13;69(7):1173-1182. doi: 10.1093/cid/ciy1021.
Pavia AT, et al. Clin Infect Dis. 2024 Mar 20;78(3):573-581.

Significance of targets

Patients and pathogens	GI PCR (n = 9,402)[a]	Stool culture, O&P, and rotavirus/adenovirus EIA (n = 5,986)[a]	P value
Patients with a pathogen	2,746/9,402 (29.2)	246/5,986 (4.1)	
Pathogens identified	3,804	251	
Viruses	1,073/2,746 (39.1)	38/246 (15.4)	0.001
Adenovirus F 40/41	89 (2.3)	5 (2.0)	0.298
Astrovirus	91 (2.4)		
Norovirus GI/GII	613 (16.1)		
Rotavirus A	176 (4.6)	35 (13.9)	0.001
Sapovirus (I, II, IV, and V)	158 (4.2)		
Bacteria	1,792/2,746 (65.3)	202/246 (82.1)	0.001
Aeromonas species		1 (0.4)	
Campylobacter species	309 (8.1)	110 (43.8)	0.001
Plesiomonas shigelloides	31 (0.8)	2 (0.8)	0.649
Salmonella species	147 (3.9)	56 (22.3)	0.001
Yersinia enterocolitica	75 (2.0)	0	0.009
Vibrio species	10 (0.3)	0	0.343
Vibrio cholerae	5 (0.1)	0	0.899
Escherichia coli subtypes	1,420/2,746 (51.7)	4/246 (1.6)	0.001
Enteroaggregative *E. coli*	530 (13.9)		
Enteropathogenic *E. coli*	863 (22.7)		
Enterotoxigenic *E.coli* (LT/ST)	167 (4.4)		
Shiga-like toxin-producing *E.coli* STX/ST2	131 (3.4)		
E. coli 0157	21 (0.6)	3 (1.2)	0.444
Shigella/enteroinvasive *E. coli*	156 (4.1)	29 (11.6)	0.001
Parasite	226/2,746 (8.2)	9/246 (3.7)	0.011
Cryptosporidium sp.	92 (2.4)	5 (2.0)	0.264
Cyclospora cayetanensis	13 (0.3)	0	0.279
Entamoeba histolytica	2 (0.1)	2 (0.8)	0.002
Giardia lamblia	125 (3.3)	2 (0.8)	0.005
Multiple pathogens	783/2,746 (28.5)	5/246 (2.0)	0.001

Axelrad et al. J Clin Microbiol 57:10.1128/jcm.01775-18

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Low risk of protozoa in bloody diarrhea samples

Pathogen	<6 months (n=12)	6-23 months (n=23)	2-4 years (n=19)	5-11 years (n=34)	12-17 years (n =23)	Total (n =111)
Bacteria						**n = 53**
Campylobacter	0 (0%)	2 (9%)	4 (21%)	1 (3%)	1 (4%)	8 (7%)
C. difficile	0 (0%)	0 (0%)	3 (16%)	3 (9%)	3 (12%)	9 (8%)
ETEC	0 (0%)	0 (0%)	1 (5%)	3 (9%)	0 (0%)	4 (3.6%)
EAEC	0 (0%)	1 (4%)	2 (11%)	7 (21%)	0 (0%)	10 (9%)
Salmonella	2 (17%)	0 (0%)	1 (5%)	3 (9%)	0 (0%)	6 (5.4%)
P. shigelloides	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)	1 (0.9%)
Vibrio	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
STEC	0 (0%)	3 (39%)	2 (11%)	4 (12%)	5 (22%)	14 (13%)
O157	0 (0%)	1 (4%)	1 (5%)	1 (3%)	2 (9%)	5 (4.5%)
Non-O157	0 (0%)	2 (9%)	1 (5%)	3 (9%)	3 (12%)	9 (8%)
Shigella/EIEC	0 (0%)	2 (9%)	2 (11%)	10 (29%)	1 (4%)	15 (14%)
Y. enterocolitica	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
V. cholerae	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Viruses						**n = 20**
Adenovirus. F	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Astrovirus	1 (8%)	2 (9%)	1 (5%)	0 (0%)	0 (0%)	4 (3.6%)
Norovirus	1 (8%)	1 (4%)	0 (0%)	1 (3%)	2 (9%)	5 (4.5%)
Sapovirus	1 (8%)	4 (17%)	1 (5%)	0 (0%)	0 (0%)	6 (5.4%)
Rotavirus. A	4 (33%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	5 (4.5%)
Protozoa						**n = 2**
Giardia	0 (0%)	0 (0%)	1 (5%)	1 (3%)	0 (0%)	2 (1.8%)
Cryptosporidium	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cyclospora	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
E. histolytica	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
No pathogen detected	4 (33%)	11 (48%)	5 (26%)	10 (29%)	12 (52%)	42 (38%)

"Among 111 children presenting with bloody diarrhea in a multicenter study of molecular testing 28 in US emergency departments, we found viral pathogens in 18%, bacteria in 48%, protozoa in 2%, and no pathogens detected in 38%."

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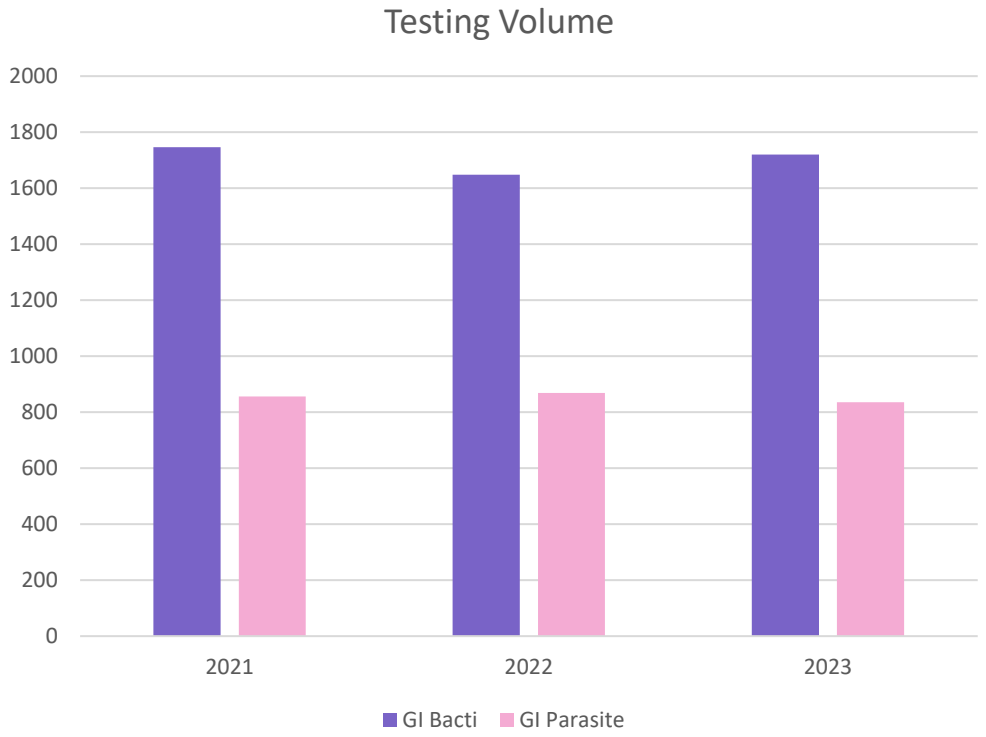
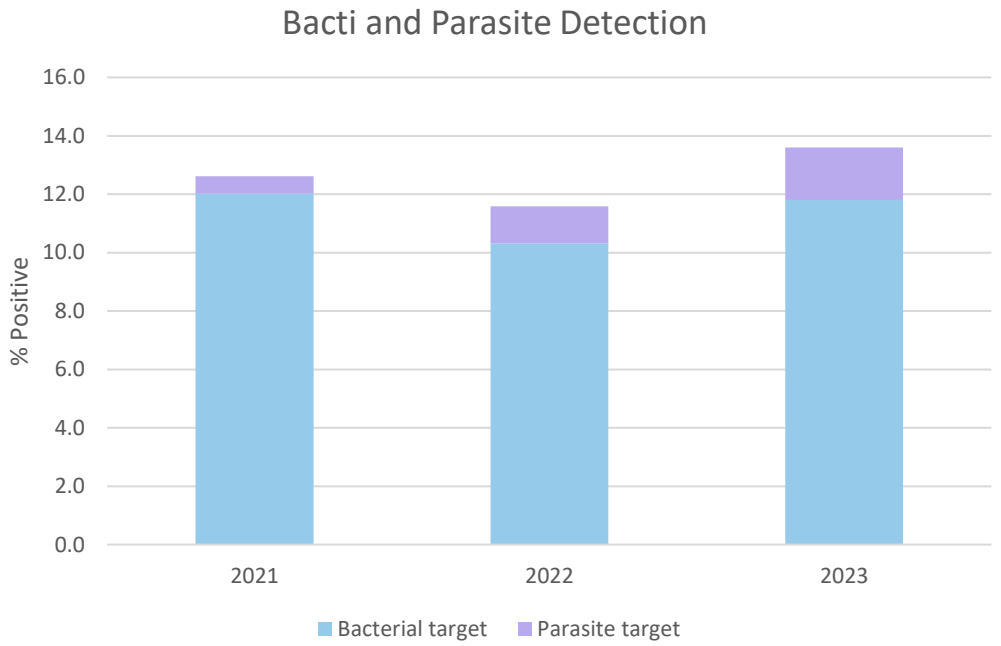
Fonseca-Romero P, et al. medRxiv [Preprint]. 2024 Apr 4:2024.04.03.24305279.

Pediatric hospital: testing volume reflects prevalence





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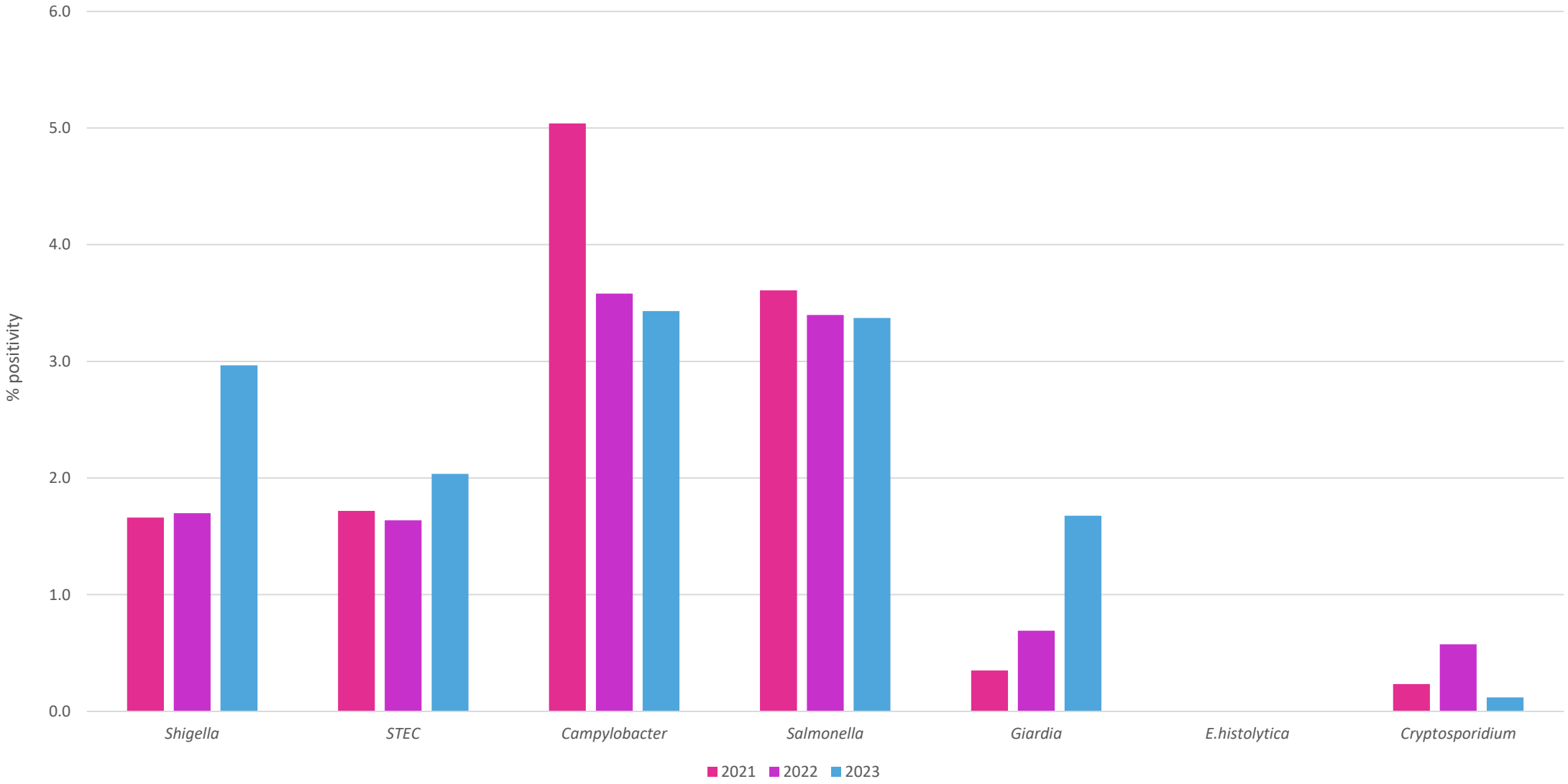
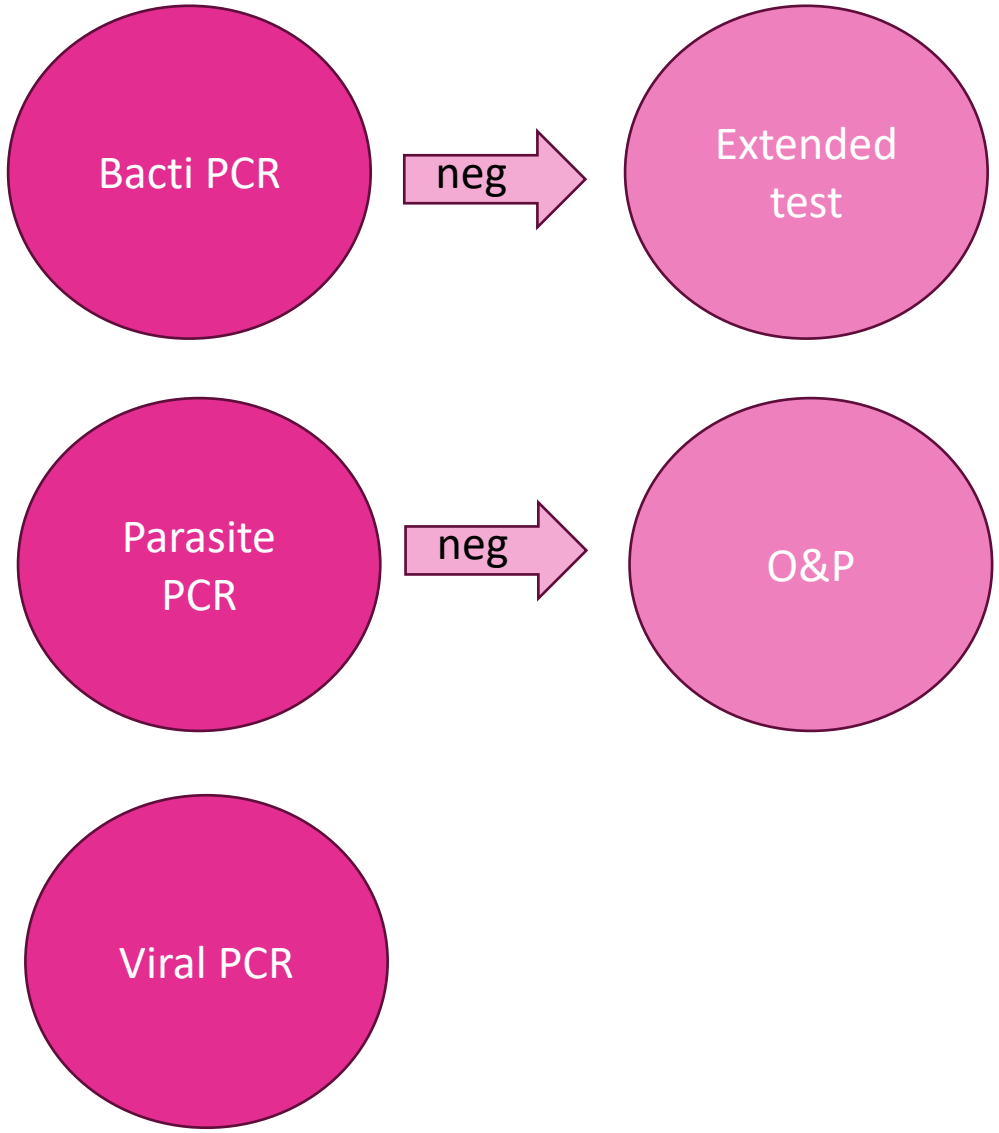

6.0
5.0
4.0
3.0
2.0
1.0
0.0
% positivity
Shigella
STEC
Campylobacter
Salmonella
Giardia
E.histolytica
Cryptosporidium
2021
2022
2023

Testing Algorithm: “a la carte option”

- Ordered based on the physician’s discretion
- Testing can be bundled or reflex approach



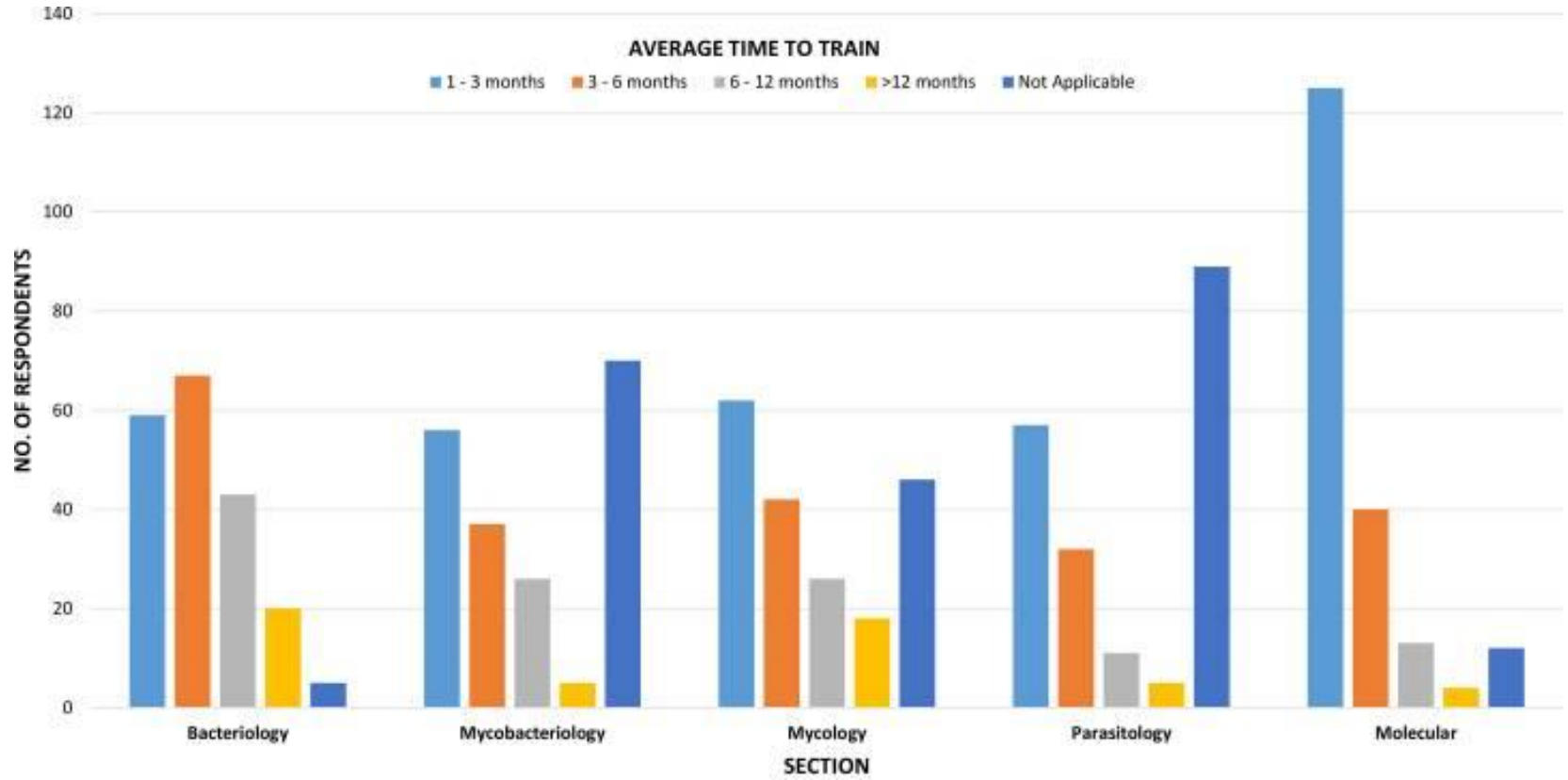
Significance of parasite panel testing

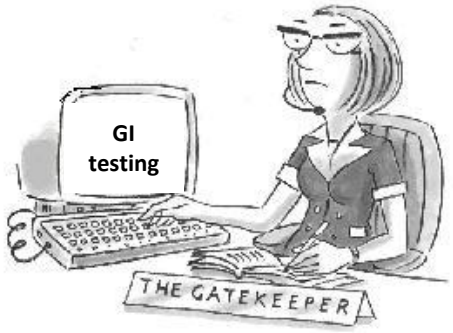
- Ova & Parasite (O&P) have become more difficult to offer as a test
- Many laboratories are currently sending samples to reference lab
- Molecular parasite panel offers solution for clinical laboratories to offer testing for the most important protozoa
- Also offers solution to re-direct MLS to other duties in the clinical laboratory
- Decrease in overall number of samples required

J Clin Microbiol. 2022 Aug; 60(8): e00241-22.
Published online 2022 Jun 6. doi: 10.1128/jcm.00241-22
PMCID: PMC9383190
PMID: 35658527

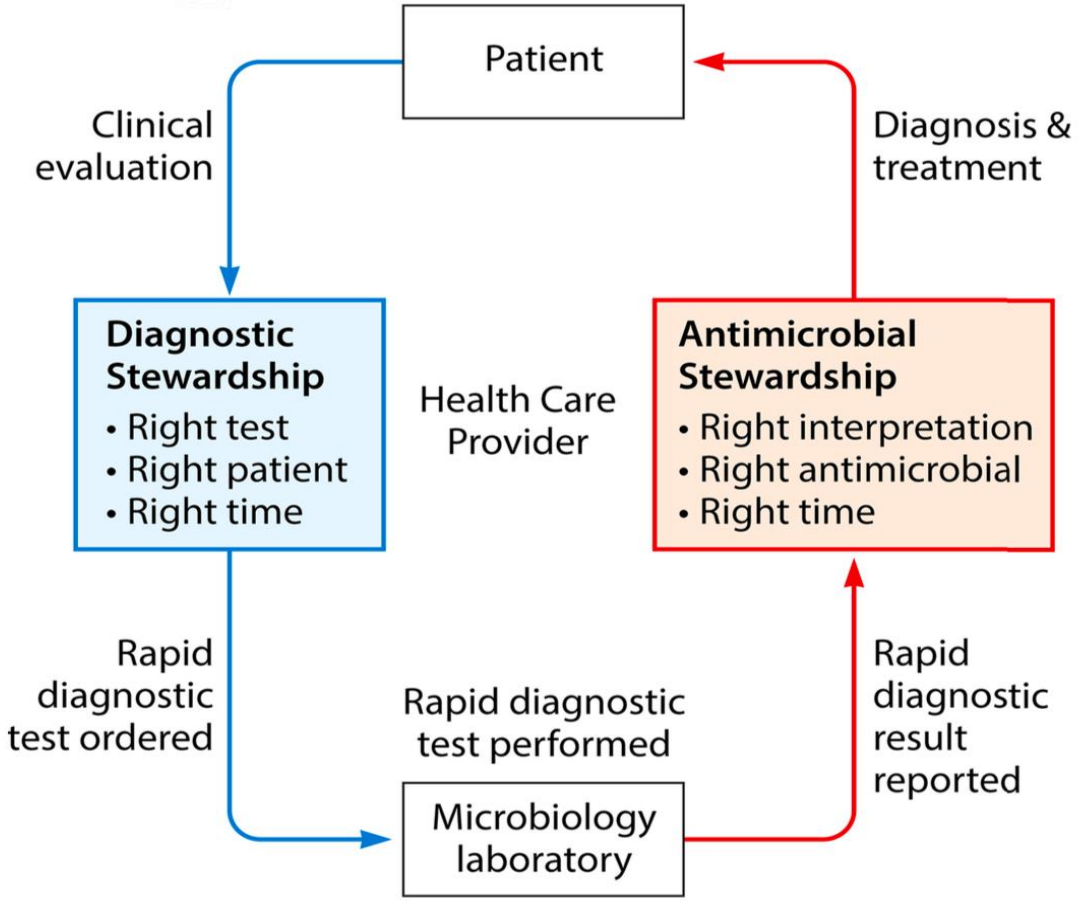
The Hidden Crisis in the Times of COVID-19: Critical Shortages of Medical Laboratory Professionals in Clinical Microbiology

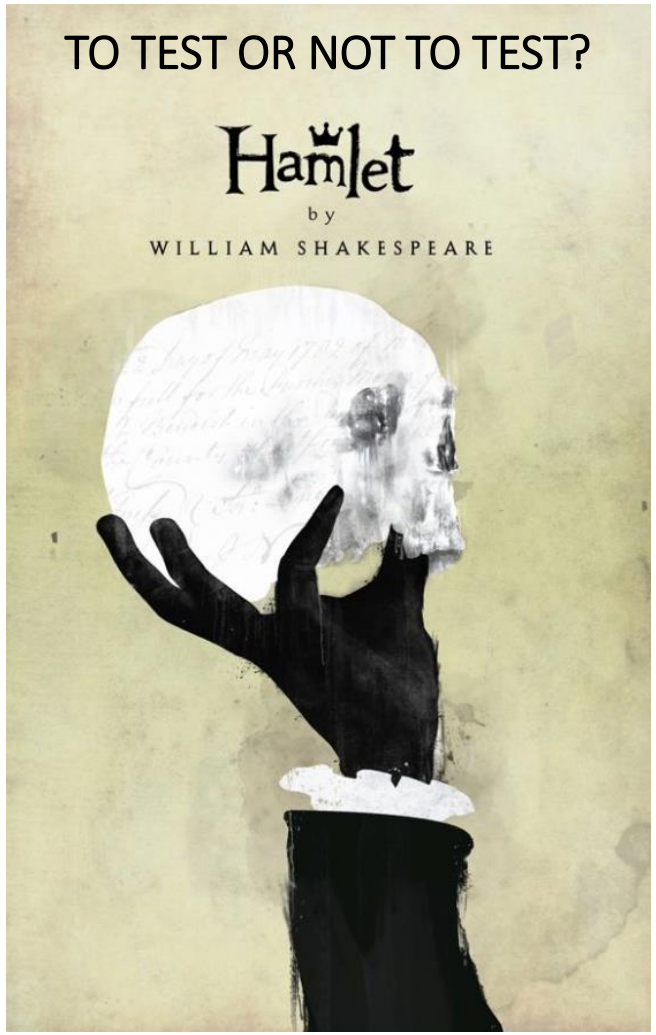
Amy L. Leber,[a,b] Ellena Peterson,[c] and Jennifer Dien Bard[d,e], **on behalf of the Personnel Standards and Workforce Subcommittee, American Society for Microbiology**





Diagnostic Stewardship





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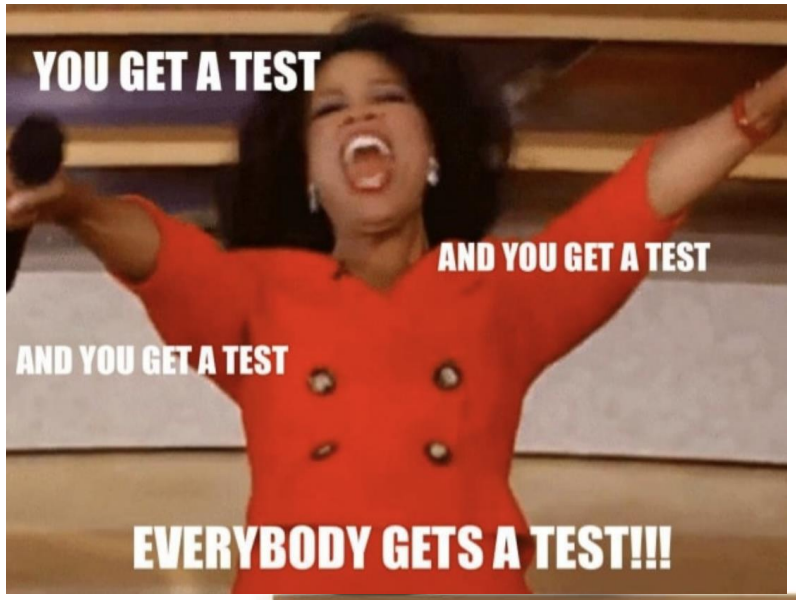
Messacar et al. J Clin Microbiol. 2017; 55(3):715-23

Finding that sweet spot



NO TEST FOR YOU

Diagnostic Stewardship = Maximizing test utility

- "To select the right test for the right patient, generating accurate, clinically relevant results at the right time to optimally influence clinical care and to conserve health care resources." Messacar et al. J Clin Microbiol. 2017; 55(3):715-23

- Will the test provide highly accurate, actionable results that can improve patient outcomes?
- Does the test potentially improve the workload in the clinical laboratory by replacing a laborious test?

- In the era of syndromic testing, the simplicity and ease of ordering and testing have led to an urgency and a "need to know" mindset

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Dien Bard J, McElvania E. Panels and Syndromic Testing in Clinical Microbiology. Clin Lab Med. 2020 Dec;40(4):393-420.

Test restrictions

- Once test is implemented, strict scrutiny must be applied to establish the most clinically relevant population to test and to optimize how the results are being communicated to the provider.

The development of support tools range from:

- Soft stops: warning for providers to reconsider whether or not the test should be ordered
- Hard stops: require providers to actively seek approval from the laboratory director
  - Example: no parasite testing in patients hospitalized for >3 days

J Community Hosp Intern Med Perspect. 2020; 10(3): 204–209.
Published online 2020 Jun 14. doi: 10.1080/20009666.2020.1760422
PMCID: PMC7426986
PMID: 32850066

An audit of inpatient stool ova and parasite (O&P) testing in a multi-hospital health system

Mohammad Qasim Khan,[a] Nicole Gentile,[a] Ying Zhou,[b] Becky A. Smith,[c] Richard B. Thomson,[d] and Eugene F. Yen[a]

Author information ▸ Copyright and License information PMC Disclaimer

- 1723 inpatient stool O&P examinations were conducted between 1 January 2013 and 31 December 2015
- 37 samples were positive for potentially pathogenic organisms, resulting in an overall yield of 2.15%
  - When *Blastocystis* was excluded as a positive test, the yield was 0.29% (5/1723)
- Total costs of conducting O&P, over the 3-year period, was ~17,868 USD, with an average of 244 hours of labor time being expended to simply examine specimens via microscopy.
- Thus, the cost per positive test was 3573.50 USD and 48 h 49 min per test when *Blastocystis* spp. were excluded as positive tests

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Khan MQ, et al. J Community Hosp Intern Med Perspect. 2020 Jun 14;10(3):204-209.

Proposed stewardship approach

- “Prevalence of gastrointestinal parasitic disease in hospitalized patients is very low and that current patterns of superfluous stool O&P testing burden both patients and the institution”
- **Risk factors:** smoking, prior parasitic disease, HIV-positive status, travel to an endemic area, and institutionalization.
- Selective testing would have reduced in-patient stool O&P examinations by 50.9%
- This would confer cost savings of 9,104.86 USD and reductions of labor time expended of 124 hours and 23 minutes over a 36-month period
- Proposal: laboratory criteria for O&P testing to necessitate the:
  - presence of at least one of the aforementioned risk factors
  - symptom duration greater than 7 days
  - specimen collection within 3 days of admission

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Khan MQ, et al. J Community Hosp Intern Med Perspect. 2020 Jun 14;10(3):204-209.

Comparative Study > Pediatrics. 2021 May;147(5):e2020036954.
doi: 10.1542/peds.2020-036954. Epub 2021 Apr 9.

Clinical Impact of a Diagnostic Gastrointestinal Panel in Children

Jillian M Cotter [1], Jacob Thomas [2], Meghan Birkholz [3], Lilliam Ambroggio [4 5], Jacqueline Holstein [6], Samuel R Dominguez [3]

- There were 12,222 stool tests performed in 8,720 patient encounters among 6,733 unique patients
- In the molecular era, there was a 21% increase in the proportion of children who underwent stool testing, a higher %positive (40% vs 11%), decreased time to result (4 vs 31 hours), and decreased time to treatment (11 vs 35 hours)
- A decrease in LOS was observed among the 3% of patients that received treatment of a bacterial and/or parasitic pathogen (5.1 vs 3.1; $P < .001$)
- In the overall population, there was no statistical difference in LOS, ancillary testing, or charges
- **Study highlight the critical need for diagnostic stewardship to optimize the value of molecular GI panels**

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Cotter JM, et al. Pediatrics. 2021 May;147(5):e2020036954.

JAMA Pediatrics | Original Investigation

Improving Antibiotic Stewardship for Diarrheal Disease With Probability-Based Electronic Clinical Decision Support

A Randomized Crossover Trial

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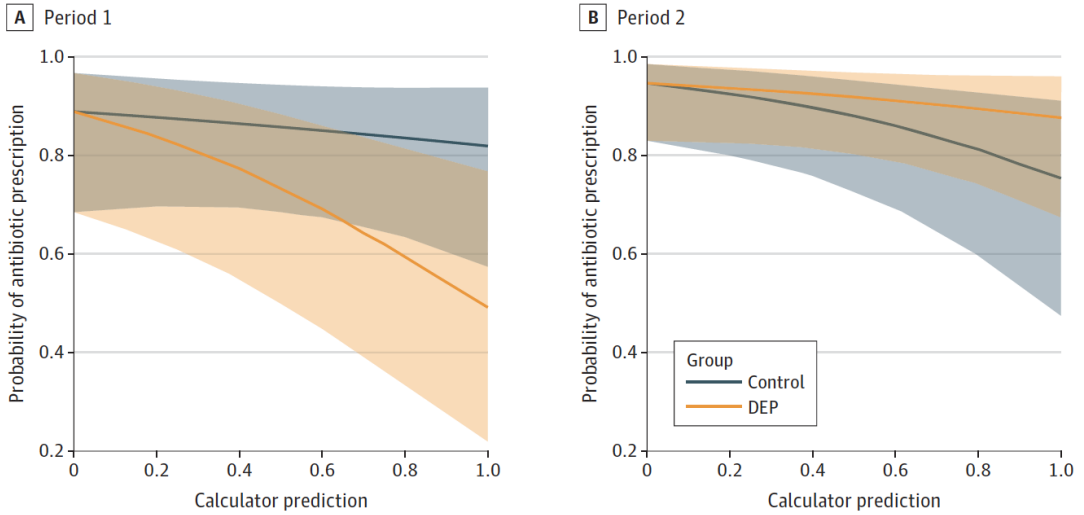
- Diarrheal etiology prediction (DEP) algorithm
- Patient-specific and location-specific features to estimate the probability that diarrhea etiology is exclusively viral
- The tool did not result in a significant change in overall antibiotic prescriptions.
- Post hoc analysis suggests that a higher predicted probability of viral etiology was linked to reductions in antibiotic use.
- ***Perhaps the tool can be used alongside with molecular panel testing?***

Table 2. Risk Differences for the Models Fit to Antibiotic Prescribing

Prescribed antibiotic	Period 1	Period 2	Full study
Models adjusted for DEP assignment			
RD (DEP minus no DEP)	−0.145	0.087	−0.042
95% CI (bootstrapped quantiles)	(−0.306 to −0.016)	(−0.028 to 0.207)	(−0.107 to 0.010)
Models adjusted for DEP predicted values			
RD (DEP minus no DEP)	−0.157	0.071	−0.056
95% CI (bootstrapped quantiles)	(−0.320 to −0.039)	(−0.038 to 0.179)	(−0.128 to −0.010)

Figure 2. Fitted Probability of Antibiotic Prescription by the Diarrheal Etiology Prediction (DEP) Probability of Viral-only Etiology, by Period



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Summary

- Molecular GI Panels allows rapid testing for patients with acute gastroenteritis that can impact care
- Benefits include increased pathogen detection, appropriate initiation or discontinuation of antibiotics and infection control procedures
- Selection of smaller vs larger molecular panels should be based on factors including the specific needs of the laboratory, budget and resources, population, prevalence and targets of interest
- To maximize the utility of molecular GI testing, diagnostic stewardship and antimicrobial stewardship is imperative

Questions??