# Accuracy and Comparison of Two Rapid Multiplex PCR Tests for Gastroenteritis Pathogens- a Systematic Review and Meta-analysis

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**Supplementary Materials S1-detailed search strategy**

The search term combination was: (Gastroenteritis OR diarrhea OR feces OR Gastrointestinal Diseases) OR (gastrointestinal OR stool OR enteric OR feces OR faeces OR diarrhea) AND (multiplex polymerase chain reaction) OR multiplex pcr OR (multiplex pcr analysis) OR (multiplex pcr assay) OR (multiplex polymerase chain reaction assay) OR (xtag OR Luminex OR Filmarray OR biofire) OR (Faecal Pathogens B OR Faecal Panel B OR ausdiagnostics) OR (gastrointestinal pathogen panel OR gastrointestinal infection panel).

Embase search strategy 2016-2019

| | |
|---|---|
| #1 | 'gastroenteritis'/exp |
| #2 | 'diarrhea'/exp |
| #3 | feces* |
| #4 | gastroenteritis* |
| #5 | 'gastrointestinal diseases*' |
| #6 | gastrointestin* OR stool* OR enteric* OR 'feces'/exp OR feces OR 'faeces'/exp OR faeces OR 'diarrhea'/exp OR diarhhrea |
| #7 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 |
| #8 | 'multiplex polymerase chain reaction'/exp |
| #9 | xtag OR 'luminex'/exp OR luminex OR 'filmarray'/exp OR filmarray OR biofire |
| #10 | 'faecal pathogens b' OR 'faecal panel b' OR ausdiagnostics |
| #11 | 'multiplex polymerase chain reaction'/exp OR 'multiplex pcr' OR 'multiplex pcr analysis' OR 'multiplex pcr assay' OR 'multiplex polymerase chain reaction' OR 'multiplex polymerase chain reaction assay' |
| #12 | 'gastrointestinal pathogen panel' OR 'gastrointestinal infection panel' |
| #13 | #8 OR #9 OR #10 OR #11 OR #12 |
| #14 | #7 AND #13 |
| #15 | #7 AND #13 AND [2016-2019]/py |
| | |

Downloaded 927

Web of Science search strategy: 2016-2019

| | | |
|---|---|---|
| #1 | TI= (multiplex* and (PCR or polymerase chain reaction or assay* or panel* or test*)) AND TS= (gastrointestin*) | |
| #2 | TS=(“gastrointestinal pathogen panel” or “gastrointestinal infection panel”) | |
| #3 | TI= (xtag or Luminex or Filmarray or biofire or “Faecal Pathogens B” or “Faecal Panel B” or ausdiagnostics) AND TS= (gastro*) | |
| #4 | #3 OR #2 OR #1 | Indexes=SCI-EXPANDED, SSCI, A&HCI<br>Timespan=All years |

| | | |
|---|---|---|
| #5 | #3 OR #2 OR #1 | Indexes=SCI-EXPANDED, SSCI, A&HCI<br>Timespan=2016-2019 |

Downloaded: 104

Pubmed search strategy: 2016-2019
(((((((("Gastroenteritis"[Mesh]) OR diarrhea*) OR feces) OR Gastroenteritis*) OR "Gastrointestinal Diseases"[Mesh]) OR ((gastrointestin[Text Word] OR stool*[Text Word] OR enteric*[Text Word] OR feces[Text Word] OR faeces[Text Word] OR diarrhea[Text Word])))) AND (((((("Multiplex Polymerase Chain Reaction"[Mesh]) OR ((xtag[Text Word] OR Luminex[Text Word] OR Filmarray[Text Word] OR biofire[Text Word]))) OR (("Faecal Pathogens B"[Text Word] OR "Faecal Panel B"[Text Word] OR ausdiagnostics[Text Word]))) OR "multiplex polymerase chain reaction" OR "multiplex pcr" OR "multiplex pcr analysis" OR "multiplex pcr assay" OR "multiplex polymerase chain reaction" OR "multiplex polymerase chain reaction assay") OR ((gastrointestinal pathogen panel[Text Word] OR gastrointestinal infection panel[Text Word])))))) AND ("2016"[Date - Completion] : "3000"[Date - Completion])
Downloaded: 546

Ovid medline search strategy: 2016-2019
Ovid MEDLINE® and In-Process & Other Non-Indexed Citations 1946 to Present

| | |
|---|---|
| 1 | exp Gastroenteritis/ |
| 2 | exp *Diarrhea/ |
| 3 | exp *Feces/ |
| 4 | exp *Gastroenteritis/ |
| 5 | exp *Gastrointestinal Diseases/ |
| 6 | (gastrointestin* or stool* or enteric* or feces or faeces or diarrh?ea).tw. |
| 7 | 1 or 2 or 3 or 4 or 5 or 6 |
| 8 | Multiplex Polymerase Chain Reaction/ |
| 9 | (xtag or Luminex or Filmarray or biofire).tw. |
| 10 | (“Faecal Pathogens B” or “Faecal Panel B” or ausdiagnostics).tw. |
| 11 | (multiplex* adj4 (PCR or polymerase chain reaction or assay* or panel* or test*)).tw. |
| 12 | (gastrointestinal pathogen panel or gastrointestinal infection panel).tw. |
| 13 | 13. 8 or 9 or 10 or 11 or 12 |
| 14 | 14. 7 and 13 |
| 15 | limit 14 to yr="2016 - 2019" |

Downloaded: 606

**Supplementary Materials S2-Guidance notes for study assessment using tailored Quality Assessment of Diagnostic Accuracy Studies-2**

Risk of bias should be judged as low for each domain only if all questions are answered with 'yes'. The risk of bias should be classed as 'high' if one or more signalling question is answered with 'no'. If at least one question is answered with 'unclear', the risk of bias should be judged 'unclear'.

| |
|---|
| ***Domain 1: patient selection*** |
| ***risk of bias*** |
| Was a consecutive or random sample of patients enrolled? |
| Was a case–control design avoided? |
| Did the study avoid inappropriate exclusions? |
| Was only one sample per episode included in the study? |
| ***Concerns regarding applicability:*** If the samples are collected from diarrhea patients, then the concerns regarding applicability should be judged as 'low'. If the study population is questionable or unconcerned, then the concerns regarding applicability should be classed as 'unclear'. If the samples are test-negative samples of conventional test, the concerns regarding applicability should be judged as 'high'. If the samples are from mixed population(such as travellers, immunocompromised patients, children aged ≤ 5 years etc.), the concerns are low. If the samples are from travellers or immunocompromised patient only, then the concerns are high. |
| |
| ***Domain 2: index test*** |
| ***risk of bias*** |
| Were the index test results interpreted without knowledge of the results of the comparator and verification method? |
| If a threshold was used, was it explicitly pre-specified? |
| Did all samples receive the index test? |
| Was the index test undertaken as recommended by the manufacturer? |
| ***Concerns regarding applicability:*** If the GI panel test is used according to the manufacturer's instructions, the concern of applicability of the index test is 'low'. |
| ***Domain 3: reference standard*** |
| ***risk of bias*** |
| Were the reference standard results interpreted without knowledge of the results of the index test and verification method? |

| |
|---|
| Is the reference standard(comparator) likely to correctly classify the target condition? |
| If a threshold was used, was it explicitly pre-specified? |
| ***Concerns regarding applicability:*** The question evaluated whether or not the target condition identified by the reference standard matches the target condition of interest in the review. The target condition for this assessment is the pathogen causing symptoms of diarrhea. If the reference standard detects pathogen DNA/RNA at levels that are unlikely to cause symptoms or detect dead organisms, then the applicability concern is high. Therefore, the concerns regarding applicability of the reference standard are 'high' if discrepant results were investigated with PCR-based methods and the comparator methods for at least some pathogens were conventional non-PCR microbiology tests. Furthermore, PCR and sequencing are not common daily practice due to their higher price, then the concerns regarding applicability are high. |
| |
| ***Domain 4: flow and timing*** |
| ***risk of bias*** |
| Was there an appropriate interval between index test(s) and reference standard? |
| Did all discordant samples receive a reference standard? |
| Did all patients receive the same reference standard? |
| Did all samples receive the comparator methods for all pathogens considered in the study? |
| Were all patients included in the analysis? |

**Supplementary Materials S3**- Characteristics of the 11 included studies (21 data sets)

| **Characteristic** | **n (data sets) (%)** |
|---|---|
| **Age** | |
| Children | 2 (10%) |
| Adult | 1 (5%) |
| Mixed | 12(56%) |
| Unclear | 6 (29%) |
| **Index test** | |
| Luminex xTAG GI panel | 15(71%) |
| FilmArray GI panel | 6 (29%) |
| **Reference standard** | |
| Sequencing or real-time PCR | 6 (29%) |
| Conventional standard microbiology techniques (including culture, C. difficile toxin study, enzyme immunoassay (EIA) or microscopy) | 6 (29%) |
| Mixed (including PCR and conventional standard microbiology techniques) | 9 (42%) |
| **Specimen type** | |
| Stool | 21(100%) |
| **Study design** | |
| Prospective | 15(71%) |
| Retrospective | 4 (19%) |
| mixed | 2 (10%) |
| **Country** | |
| United States | 9 (42%) |

| | |
|---|---|
| Netherlands | 5 (23%) |
| Spain | 2 (10%) |
| Vietnam | 2 (10%) |
| United Kingdom | 1 (5%) |
| France | 1 (5%) |
| China | 1 (5%) |

**Supplementary Materials S4**- Comparison of characteristics between two FDA-approved multiplex platforms for the detection of gastrointestinal pathogens. (10)

| **Feature** | **Luminex** | **FilmArray** |
|---|---|---|
| Technology | PCR plus xTAG (fluorescent bead-based detection) | Nested PCR plus melting curve |
| Processing time per run (min) | 45 | 2 |
| Separate extraction required (min) | Yes (~45) | No |
| Time/run (h) | ~3.5 | ~1 |
| Throughput (no. specimens/run) | 96 | 1 |
| Maximum no. of targets | 15 | 22 |
| targets | ● *Campylobacter* (*C. jejuni, C. coli*和*C. lari*)<br>● *Clostridium difficile (C. difficile)* toxin A/B<br>● *Escherichia coli (E. coli)* O157<br>● Enterotoxigenic *Escherichia coli* (ETEC) LT/ST<br>● *Salmonella*<br>● Shiga-like Toxin producing *E. coli* (STEC) stx 1/stx 2<br>● *Shigella (*including *S. boydii, S. sonnei, S. flexneri and S. dysenteriae*)<br>● *Vibrio cholerae (V. cholerae)* cholera toxin gene (ctx)<br>● *Yersinia enterocolitica*<br>● Adenovirus 40/41<br>● Norovirus GI/GII<br>● Rotavirus A<br>● *Cryptosporidium* (*C. parvum and C. hominis*)<br>● *Entamoeba histolytica*<br>● *Giardia lamblia* | ● Campylobacter (C. jejuni/C. coli/C. upsaliensis)<br>● Clostridium difficile (C. difficile) toxin A/B<br>● Plesiomonas shigelloides<br>● Salmonella<br>● Vibrio (V. parahaemolyticus/V. vulnificus/ V. cholerae)<br>● Vibrio cholerae<br>● Yersinia enterocolitica<br>● Enteroaggregative Escherichia coli (EAEC)<br>● Enteropathogenic Escherichia coli (EPEC)<br>● Enterotoxigenic Escherichia coli (ETEC) lt/st<br>● Shiga-like toxin-producing Escherichia coli (STEC) stx1/stx2<br>● E. coli O157<br>● Shigella/ Enteroinvasive Escherichia coli (EIEC)<br>● Adenovirus F 40/41<br>● Astrovirus<br>● Norovirus GI/GII<br>● Rotavirus A |

| **Feature** | **Luminex** | **FilmArray** |
|---|---|---|
| | | • Sapovirus (Genogroups I, II, IV and V)<br>• *Cryptosporidium*<br>• *Cyclospora cayetanensis*<br>• *Entamoeba histolytica*<br>• *Giardia lamblia* |
| Open or closed system | Open | Closed |
| Results | Qualitative | Qualitative |
| Footprint size | Moderate | Small |
| List price per instrument ($) | 37,000 | 39,500 |
| List price reagent cost per specimen ($) | 80–90 | 155 |

**Supplementary Materials S5**-detailed characteristics of 11 included studies

| ID | Author, year, country | Number and characteristics of samples and patient | Patient age | Patient inclusion criteria | Specimen type | Routine testing methods | Adjudication methods for discordant results | Index test (multiplex PCR) | *pathogens* | Sen | Spe |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Deng J et al., 2015, China | Prospective, 290 stool samples from 290 patient. 70 inpatients and 220 outpatients, and pediatric outpatients were the most common (54.1%). 64.1% male. | Mixed (median age of 25 months and ranging from 11 days to 83 years.) | Diarrheal patients | Stool | Bacterial culture, serotyping for Salmonella and Shigella, real-time reverse transcription-polymerase chain reaction (RT-PCR) assays for viral detection, microscopic examination for parasite detection. | Singleplex PCR and sequencing | Luminex xTAG | *Campylobacter* | 1.00 | 1.00 |
| | | | | | | | | | *C. difficile toxin A* | 1.00 | 0.99 |
| | | | | | | | | | *C. difficile toxin B* | 0.87 | 1.00 |
| | | | | | | | | | *E. coli O157* | 1.00 | 1.00 |
| | | | | | | | | | *ETEC LT/ST* | 1.00 | 1.00 |
| | | | | | | | | | *Salmonella* | 0.85 | 0.99 |
| | | | | | | | | | *Shigella* | 1.00 | 1.00 |
| | | | | | | | | | *V. cholerae* | NA | 1.00 |
| | | | | | | | | | *Yersinia enterocolitica* | 1.00 | 1.00 |
| | | | | | | | | | *Adenovirus 40/41* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GII* | 1.00 | 0.99 |
| | | | | | | | | | *Rotavirus A* | 1.00 | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | NA | 1.00 |
| 2 | Chhabra P et al., 2017, USA | Retrospective, 300 stool samples from children and adults | Unclear | Patient with acute | Stool | TAC system, real-time PCR and sequencing | Discordant analysis | Luminex xTAG | *Adenovirus 40/41* | 0.58 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.78 | 1.00 |
| | | | | | | | | | *Rotavirus A* | 0.96 | 1.00 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | gastroenteritis | | | | FilmArray | *Adenovirus F 40/41* | 0.97 | 0.98 |
| | | | | | | | | | *Astrovirus* | 0.97 | 0.99 |
| | | | | | | | | | *Norovirus GI/GII* | 0.88 | 1.00 |
| | | | | | | | | | *Rotavirus A* | 1.00 | 0.96 |
| | | | | | | | | | *Sapovirus* | 0.98 | 1.00 |
| 3 | Alejo-Cancho I et al., 2017, Spain | Prospective, 95 stool samples were obtained from 95 immunocompromised adult patients. | Adult patient, with a median age of 52 years (46–64). | Acute diarrheal patient | Stool | Routine microbiological techniques, including bacterial culture, C. difficile toxin study, microsoopy for parasite, virus antigen. | Second multiplex assay (Allplex, Seegene, Korea) | FilmArray | *Campylobacter* | 1.00 | 1.00 |
| | | | | | | | | | *C. difficile toxin A/B* | 1.00 | 1.00 |
| | | | | | | | | | *Plesiomonas shigelloides* | NA | 1.00 |
| | | | | | | | | | *Salmonella* | 1.00 | 1.00 |
| | | | | | | | | | *Vibrio spp.* | NA | 1.00 |
| | | | | | | | | | *Vibrio cholerae* | NA | 1.00 |
| | | | | | | | | | *Yersinia enterocolitica* | NA | 1.00 |
| | | | | | | | | | *EAEC* | 1.00 | 1.00 |
| | | | | | | | | | *EPEC* | 1.00 | 0.97 |
| | | | | | | | | | *ETEC lt/st* | 1.00 | 1.00 |
| | | | | | | | | | *STEC stx1/stx2* | NA | 1.00 |
| | | | | | | | | | *E. coli O157* | NA | 1.00 |
| | | | | | | | | | *Shigella/EIEC* | NA | 1.00 |
| | | | | | | | | | *Adenovirus F 40/41* | 0.00 | 1.00 |
| | | | | | | | | | *Astrovirus* | NA | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 1.00 | 1.00 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *Rotavirus A* | 1.00 | 1.00 |
| | | | | | | | | | *Sapovirus* | NA | 1.00 |
| | | | | | | | | | *Cryptosporidium* | NA | 1.00 |
| | | | | | | | | | *Cyclospora cayetanensis* | NA | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 1.00 |
| 4 | Duong VT et al., 2016, Vietnam | Retrospective, 479 stool samples were collected from 92 adults (>15 years) and 387 children (≤15 years old) admitted to the hospital with diarrheal disease. | The median age of the adult patients was 50 years (interquartile range [IQR], 33 to 64 years). In children, the median age was 16.5 months (IQR, 6.7 to 20 months). | Diarrheal patients | Stool | Microbiological culture and real-time PCR | Discordant analysis | Luminex xTAG | *Campylobacter* | 0.91 | 0.99 |
| | | | | | | | | | *C. difficile toxin A* | NA | NA |
| | | | | | | | | | *C. difficile toxin B* | NA | NA |
| | | | | | | | | | *E. coli O157* | NA | NA |
| | | | | | | | | | *ETEC LT/ST* | NA | NA |
| | | | | | | | | | *Salmonella* | 0.90 | 0.67 |
| | | | | | | | | | *STEC stx1/stx2* | NA | NA |
| | | | | | | | | | *Shigella* | 0.96 | 0.99 |
| | | | | | | | | | *V. cholerae* | NA | NA |
| | | | | | | | | | *Yersinia enterocolitica* | NA | NA |
| | | | | | | | | | *Adenovirus 40/41* | 0.92 | 0.99 |
| | | | | | | | | | *Norovirus GI* | 0.88 | 0.99 |
| | | | | | | | | | *Norovirus GII* | 0.97 | 0.99 |
| | | | | | | | | | *Rotavirus A* | 0.93 | 0.99 |
| | | | | | | | | | *Cryptosporidium* | NA | NA |
| | | | | | | | | | *Entamoeba histolytica* | NA | NA |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *Giardia lamblia* | NA | NA |
| | | | | | | | | | *Campylobacter* | 0.90 | 0.92 |
| | | | | | | | | | *Salmonella* | 0.95 | 0.61 |
| | | | | | | | | | *Shigella* | 1.00 | 0.88 |
| 6 | Khare R et al., 2014, USA | Prospective and retrospective, 230 prospectively collected samples | Unclear | Stool samples submitted to laboratory for routine GI testing. | Stool | Routine testing (e.g., culture, microscopy, antigen testing, and/or individual real-time PCR) | Discordant analysis | Luminex xTAG | *Campylobacter* | 1.00 | 1.00 |
| | | | | | | | | | *C. difficile toxin A/B* | 0.96 | 0.97 |
| | | | | | | | | | *E. coli O157* | NA | 1.00 |
| | | | | | | | | | *ETEC LT/ST* | 1.00 | 1.00 |
| | | | | | | | | | *Salmonella* | 1.00 | 1.00 |
| | | | | | | | | | *STEC stx1/stx2* | NA | 1.00 |
| | | | | | | | | | *Shigella* | 1.00 | 1.00 |
| | | | | | | | | | *V. cholerae* | NA | 1.00 |
| | | | | | | | | | *Yersinia enterocolitica* | NA | 1.00 |
| | | | | | | | | | *Adenovirus 40/41* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 1.00 | 0.91 |
| | | | | | | | | | *Rotavirus A* | NA | 0.99 |
| | | | | | | | | | *Cryptosporidium* | 1.00 | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 1.00 |
| 6 | Khare R et al., 2014, USA | Prospective and retrospective, 270 additional previously characterized samples | Unclear | Stool samples submitted to laborator | Stool | Routine testing (e.g., culture, microscopy, antigen testing, and/or | Discordant analysis | Luminex xTAG | *Campylobacter* | 0.79 | 1.00 |
| | | | | | | | | | *C. difficile toxin A/B* | 0.92 | 0.98 |
| | | | | | | | | | *E. coli O157* | 0.91 | 1.00 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | y for routine GI testing. | | individual real-time PCR) | | | *ETEC LT/ST* | NA | NA |
| | | | | | | | | | *Salmonella* | 0.83 | 1.00 |
| | | | | | | | | | *STEC stx1/stx2* | 0.96 | 1.00 |
| | | | | | | | | | *Shigella* | 0.82 | NA |
| | | | | | | | | | *V. cholerae* | NA | NA |
| | | | | | | | | | *Yersinia enterocolitica* | 0.48 | 1.00 |
| | | | | | | | | | *Adenovirus 40/41* | 0.80 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.93 | 0.86 |
| | | | | | | | | | *Rotavirus A* | 0.93 | 1.00 |
| | | | | | | | | | *Cryptosporidium* | 1.00 | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | 1.00 | 1.00 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 1.00 |
| 6 | Khare R et al., 2014, USA | Prospective, 230 prospectively collected samples | Unclear | Stool samples submitted to laboratory for routine GI testing. | Stool | Routine testing (e.g., culture, microscopy, antigen testing, and/or individual real-time PCR) | Discordant analysis | FilmArray | *Campylobacter* | 1.00 | 1.00 |
| | | | | | | | | | *C. difficile toxin A/B* | 1.00 | 0.97 |
| | | | | | | | | | *Plesiomonas shigelloides* | NA | 1.00 |
| | | | | | | | | | *Salmonella* | 1.00 | 1.00 |
| | | | | | | | | | *Vibrio spp.* | NA | 1.00 |
| | | | | | | | | | *Vibrio cholerae* | NA | 1.00 |
| | | | | | | | | | *Yersinia enterocolitica* | NA | 1.00 |
| | | | | | | | | | *EAEC* | NA | NA |
| | | | | | | | | | *EPEC* | NA | NA |
| | | | | | | | | | *ETEC lt/st* | 1.00 | 1.00 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *STEC stx1/stx2* | NA | 1.00 |
| | | | | | | | | | *E. coli O157* | NA | 1.00 |
| | | | | | | | | | *Shigella/EIEC* | 1.00 | 1.00 |
| | | | | | | | | | *Adenovirus F 40/41* | 1.00 | 1.00 |
| | | | | | | | | | *Astrovirus* | 1.00 | NA |
| | | | | | | | | | *Norovirus GI/GII* | 0.92 | 1.00 |
| | | | | | | | | | *Rotavirus A* | NA | 1.00 |
| | | | | | | | | | *Sapovirus* | 1.00 | NA |
| | | | | | | | | | *Cryptosporidium* | 1.00 | 1.00 |
| | | | | | | | | | *Cyclospora cayetanensis* | NA | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 1.00 |
| | | | | | | | | | *Aeromonas spp.* | 1.00 | 1.00 |
| 6 | Khare R et al., 2014, USA | Prospective, 270 additional previously characterized samples | Unclear | Stool samples submitted to laboratory for routine GI testing. | Stool | Routine testing (e.g., culture, microscopy, antigen testing, and/or individual real-time PCR) | Discordant analysis | FilmArray | *Campylobacter* | 0.97 | 1.00 |
| | | | | | | | | | *C. difficile toxin A/B* | 0.92 | 0.98 |
| | | | | | | | | | *Plesiomonas shigelloides* | 1.00 | 1.00 |
| | | | | | | | | | *Salmonella* | 1.00 | 1.00 |
| | | | | | | | | | *Vibrio spp.* | NA | NA |
| | | | | | | | | | *Vibrio cholerae* | NA | NA |
| | | | | | | | | | *Yersinia enterocolitica* | 1.00 | 1.00 |
| | | | | | | | | | *EAEC* | NA | NA |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *EPEC* | NA | NA |
| | | | | | | | | | *ETEC lt/st* | NA | NA |
| | | | | | | | | | *STEC stx1/stx2* | 1.00 | 0.99 |
| | | | | | | | | | *E. coli O157* | 1.00 | 1.00 |
| | | | | | | | | | *Shigella/EIEC* | 0.91 | 1.00 |
| | | | | | | | | | *Adenovirus F 40/41* | 0.90 | 0.99 |
| | | | | | | | | | *Astrovirus* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.93 | 1.00 |
| | | | | | | | | | *Rotavirus A* | 1.00 | 1.00 |
| | | | | | | | | | *Sapovirus* | 0.90 | 1.00 |
| | | | | | | | | | *Cryptosporidium* | 1.00 | 1.00 |
| | | | | | | | | | *Cyclospora cayetanensis* | NA | NA |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 1.00 |
| | | | | | | | | | *Aeromonas spp.* | 0.24 | 1.00 |
| 7 | Buss SN et al., 2015, USA | Prospective, 1556 stool samples from 584 adult (older than 21 years old [38%]) and 972 pediatric (younger than or equal to 21 years old [62%]) populations | Unclear | Stool samples submitted with orders by the provider for stool culture | Stool | Stool culture, PCR | Discordant analysis | FilmArray | *Campylobacter* | 0.97 | 0.98 |
| | | | | | | | | | *C. difficile toxin A/B* | 0.99 | 0.97 |
| | | | | | | | | | *Plesiomonas shigelloides* | 1.00 | 0.99 |
| | | | | | | | | | *Salmonella* | 1.00 | 1.00 |
| | | | | | | | | | *Vibrio spp.* | NA | 1.00 |
| | | | | | | | | | *Vibrio cholerae* | NA | 1.00 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *Yersinia enterocolitica* | NA | 1.00 |
| | | | | | | | | | *EAEC* | 0.99 | 0.98 |
| | | | | | | | | | *EPEC* | 0.99 | 0.97 |
| | | | | | | | | | *ETEC lt/st* | 1.00 | 0.99 |
| | | | | | | | | | *STEC stx1/stx2* | 1.00 | 1.00 |
| | | | | | | | | | *E. coli O157* | 1.00 | 0.97 |
| | | | | | | | | | *Shigella/EIEC* | 0.96 | 1.00 |
| | | | | | | | | | *Adenovirus F 40/41* | 0.96 | 1.00 |
| | | | | | | | | | *Astrovirus* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.95 | 0.99 |
| | | | | | | | | | *Rotavirus A* | 1.00 | 0.99 |
| | | | | | | | | | *Sapovirus* | 1.00 | 0.99 |
| | | | | | | | | | *Cryptosporidium* | 1.00 | 1.00 |
| | | | | | | | | | *Cyclospora cayetanensis* | 1.00 | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 1.00 |
| 8 | Claas EC et al., 2013, Netherlands | Prospective, 901 stool specimens from both pediatric and adult patients | Unclear | Stool collected in four hospitals | Stool | Routine testing (e.g., culture, microscopy, EIA/DFA, or real-time PCR) | Discordant analysis | Luminex xTAG | *Campylobacter* | 1.00 | 0.82 |
| | | | | | | | | | *C. difficile toxin A/B* | 1.00 | 0.91 |
| | | | | | | | | | *E. coli O157* | 0.83 | 0.99 |
| | | | | | | | | | *ETEC LT/ST* | NA | 1.00 |
| | | | | | | | | | *Salmonella* | 0.97 | 0.95 |

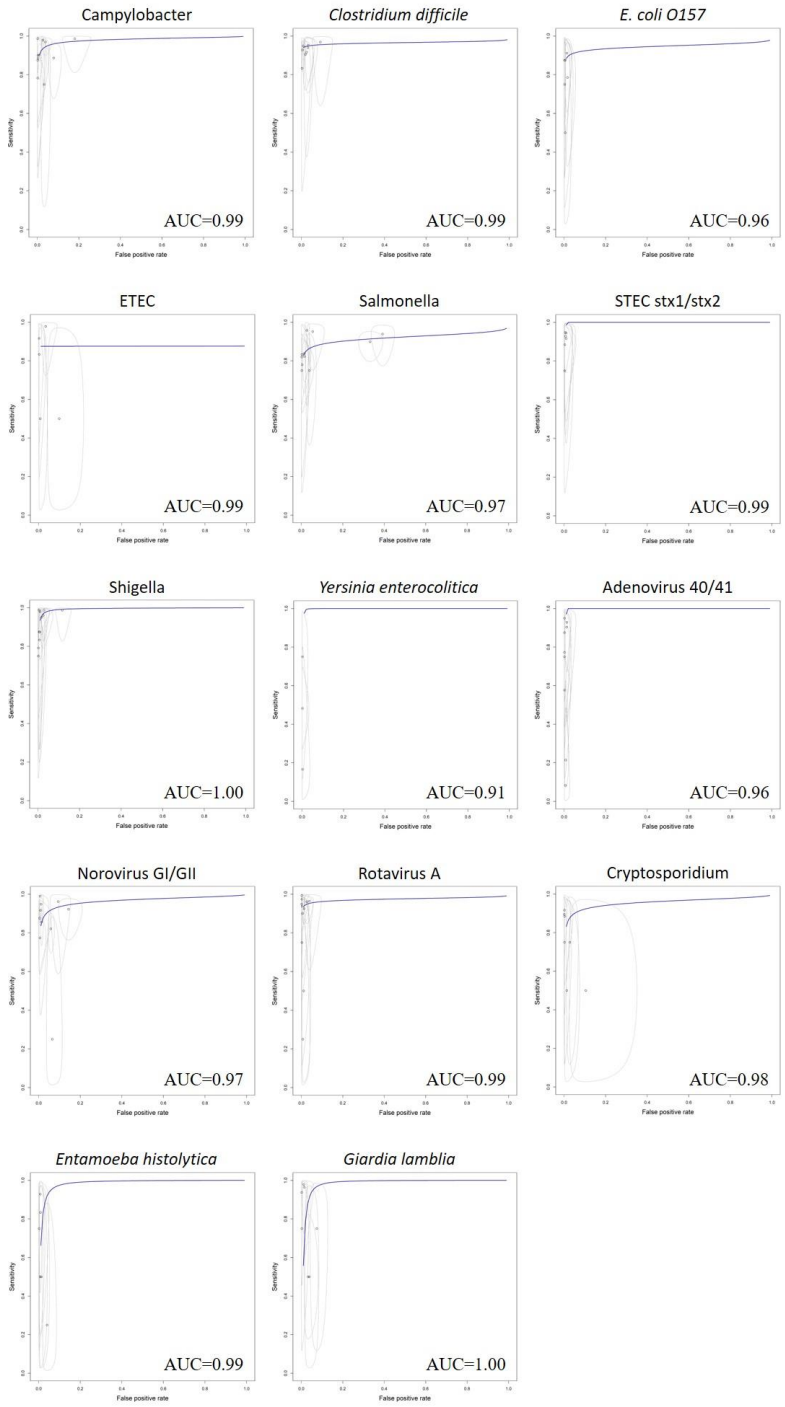
| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *STEC stx1/stx2* | 1.00 | 1.00 |
| | | | | | | | | | *Shigella* | 0.97 | 0.98 |
| | | | | | | | | | *V. cholerae* | NA | 1.00 |
| | | | | | | | | | *Yersinia enterocolitica* | 0.00 | 1.00 |
| | | | | | | | | | *Adenovirus 40/41* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI* | NA | 1.00 |
| | | | | | | | | | *Norovirus GII* | 1.00 | 0.99 |
| | | | | | | | | | *Rotavirus A* | 0.00 | 1.00 |
| | | | | | | | | | *Cryptosporidium* | NA | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | NA | 0.96 |
| | | | | | | | | | *Adenovirus F 40/41* | 0.20 | 0.99 |
| | | | | | | | | | *Astrovirus* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.93 | 0.98 |
| | | | | | | | | | *Rotavirus A* | 1.00 | 1.00 |
| | | | | | | | | | *Cryptosporidium* | 0.91 | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | 1.00 | 0.99 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 0.99 |
| | | | | | | | | | *Campylobacter* | 0.97 | 0.96 |
| | | | | | | | | | *E. coli O157* | 0.94 | 0.99 |
| | | | | | | | | | *Salmonella* | 0.83 | 0.99 |
| | | | | | | | | | *Shigella* | 1.00 | 0.97 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *V. cholerae* | 0.00 | 1.00 |
| | | | | | | | | | *Yersinia enterocolitica* | NA | 1.00 |
| | | | | | | | | | *Cryptosporidium* | 0.92 | 1.00 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 0.99 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 0.97 |
| | | | | | | | | | *C. difficile toxin A/B* | 0.97 | 0.97 |
| | | | | | | | | | *ETEC lt/st* | NA | 0.91 |
| | | | | | | | | | *STEC stx1/stx2* | 1.00 | 0.99 |
| | | | | | | | | | *Cryptosporidium* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | NA | 1.00 |
| 9 | Halligan E et al., 2014, UK | Prospective, 2187 diarrhoeal stool samples. 986 (45%) samples originated from inpatients developing symptoms in the first 4 days of admission or from outpatient clinics, and the remaining 1201 (55%) samples were from inpatients on day 4 or more of admission. | Unclear | Diarrheal patients | Stool | Conventional tests including microbiological culture, microscopy, microwell enzyme immunoassay, immunochromatographic test | Discordant analysis | Luminex xTAG | *Campylobacter* | 1.00 | 0.97 |
| | | | | | | | | | *C. difficile toxin A/B* | 0.95 | 0.99 |
| | | | | | | | | | *E. coli O157* | 1.00 | 1.00 |
| | | | | | | | | | *ETEC LT/ST* | NA | NA |
| | | | | | | | | | *Salmonella* | 1.00 | 0.97 |
| | | | | | | | | | *STEC stx1/stx2* | NA | NA |
| | | | | | | | | | *Shigella* | 1.00 | 0.99 |
| | | | | | | | | | *V. cholerae* | NA | NA |
| | | | | | | | | | *Yersinia enterocolitica* | NA | NA |
| | | | | | | | | | *Adenovirus 40/41* | 1.00 | 0.99 |
| | | | | | | | | | *Norovirus GI/GII* | 0.83 | 0.94 |

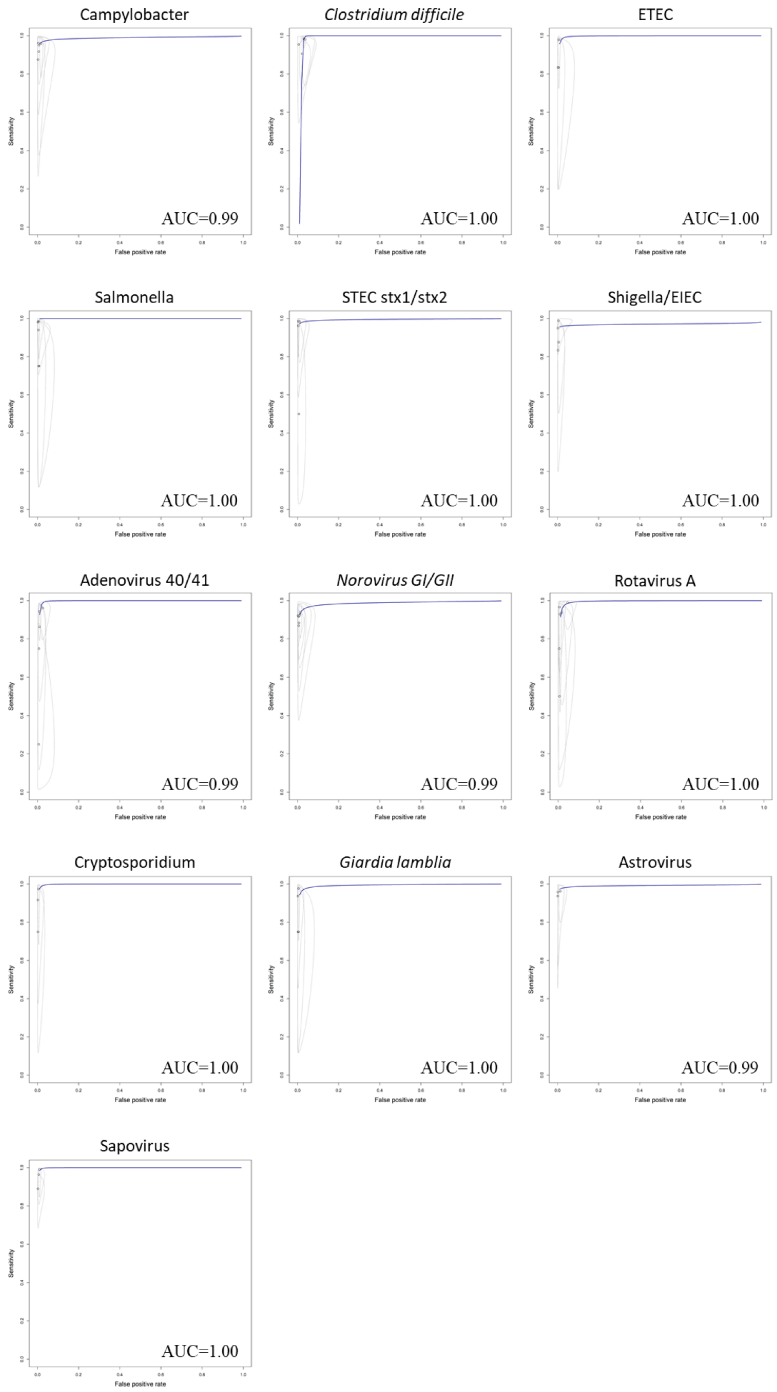
| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *Rotavirus A* | 1.00 | 0.96 |
| | | | | | | | | | *Cryptosporidium* | 1.00 | 0.97 |
| | | | | | | | | | *Entamoeba histolytica* | 0.00 | 0.96 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 0.93 |
| 10 | Mengelle C et al., 2013, France | Prospective, 440 stool samples collected from 329 diarrhoeic patients | Three groups included immunosuppressed hospitalized patients: 102 adult organ transplant recipients (mean age, 50.6; median, 56; range, 17–75), 50 immunosuppressed children (mean age, 5; median, 7; range, 0–14) and 56 children attending the neonatal unit (aged under 1 year). The 121 children attending the | Diarrheal patients | Stool | Routine diagnostic methods (e.g., culture, microscopy, immunochromatographic assay, and multiplex PCR) | Discordant analysis | Luminex xTAG | *Campylobacter* | 1.00 | 0.97 |
| | | | | | | | | | *C. difficile toxin A/B* | 1.00 | 0.98 |
| | | | | | | | | | *E. coli O157* | NA | 1.00 |
| | | | | | | | | | *ETEC LT/ST* | NA | 1.00 |
| | | | | | | | | | *Salmonella* | 0.78 | 0.96 |
| | | | | | | | | | *STEC stx1/stx2* | 1.00 | 0.99 |
| | | | | | | | | | *Shigella* | 1.00 | 1.00 |
| | | | | | | | | | *V. cholerae* | NA | 1.00 |
| | | | | | | | | | *Yersinia enterocolitica* | NA | 1.00 |
| | | | | | | | | | *Adenovirus 40/41* | 0.00 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.00 | 0.94 |
| | | | | | | | | | *Rotavirus A* | 0.97 | 0.97 |
| | | | | | | | | | *Cryptosporidium* | NA | 0.99 |
| | | | | | | | | | *Entamoeba histolytica* | NA | 1.00 |
| | | | | | | | | | *Giardia lamblia* | NA | 1.00 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | emergency unit (mean age, 2.80; median, 9; range, 0–16) were considered to be outpatients. | | | | | | | | |
| 11 | Zboromyrska Y et al., 2014, Spain | Prospective, 185 stool samples from patients with traveller's diarrhea. | Unclear | Patients with traveller's diarrhea | Stool | Routine diagnostic methods (e.g., culture, microscopy, mass spectrometry, and multiplex PCR) | Conventional PCR and bidirectional sequencing | Luminex xTAG | *Campylobacter* | 1.00 | 1.00 |
| | | | | | | | | | *C. difficile toxin A/B* | NA | 1.00 |
| | | | | | | | | | *E. coli O157* | 1.00 | 1.00 |
| | | | | | | | | | *ETEC LT/ST* | 1.00 | 0.97 |
| | | | | | | | | | *Salmonella* | 1.00 | 1.00 |
| | | | | | | | | | *STEC stx1/stx2* | 1.00 | 1.00 |
| | | | | | | | | | *Shigella* | 1.00 | 0.99 |
| | | | | | | | | | *V. cholerae* | NA | NA |
| | | | | | | | | | *Yersinia enterocolitica* | NA | NA |
| | | | | | | | | | *Adenovirus 40/41* | NA | NA |
| | | | | | | | | | *Norovirus GI/GII* | NA | 0.99 |
| | | | | | | | | | *Rotavirus A* | NA | 1.00 |
| | | | | | | | | | *Cryptosporidium* | NA | NA |
| | | | | | | | | | *Entamoeba histolytica* | 1.00 | 0.99 |
| | | | | | | | | | *Giardia lamblia* | 1.00 | 0.99 |
| | | | Unclear | | Stool | | | | *Campylobacter* | 0.92 | 1.00 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 12 | Huang RS et al., 2016, USA | 98 retrospective and 54 prospective samples collected from pediatric patients with signs and symptoms of acute gastroenteritis. | | Patient with acute gastroenteritis | | Conventional testing including stool cultures, immunochromatographic rapid tests, and singleplex RT-PCR | Discordant analysis | Luminex xTAG | *Salmonella* | 0.79 | 1.00 |
| | | | | | | | | | *STEC stx1/stx2* | 0.92 | 1.00 |
| | | | | | | | | | *Shigella* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.90 | 1.00 |
| | | | | | | | | | *Rotavirus A* | 1.00 | 1.00 |
| 12 | Huang RS et al., 2016, USA | 98 retrospective and 54 prospective samples collected from pediatric patients with signs and symptoms of acute gastroenteritis. | Unclear | Patient with acute gastroenteritis | stool | Conventional testing including stool cultures, immunochromatographic rapid tests, and singleplex RT-PCR | Discordant analysis | FilmArray | *Campylobacter* | 1.00 | 1.00 |
| | | | | | | | | | *Salmonella* | 0.96 | 1.00 |
| | | | | | | | | | *STEC stx1/stx2* | 1.00 | 1.00 |
| | | | | | | | | | *Shigella* | 1.00 | 1.00 |
| | | | | | | | | | *Norovirus GI/GII* | 0.95 | 0.99 |
| | | | | | | | | | *Rotavirus A* | 1.00 | 0.99 |



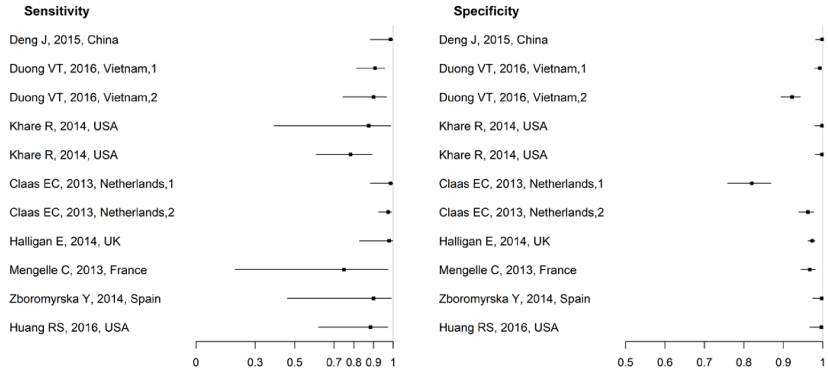

**Supplementary materials S6.** Receiver operating curve (ROC) analysis of Luminex xTAG GI panel for detection of different pathogens. The blue lines indicate the receiver operating curve. The blue lines indicate the receiver operating curve. The grey dots represent estimates of individual studies and grey circles around the dots represent the 95% confidence interval.



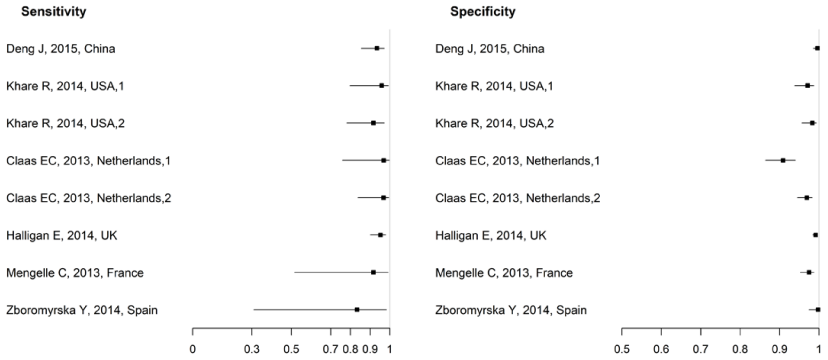

**Supplementary materials S7.** Receiver operating curve (ROC) analysis of FilmArray GI panel for detection of different pathogens. The blue lines indicate the receiver operating curve. The blue lines indicate the receiver operating curve. The grey dots represent estimates of individual studies and grey circles around the dots represent the 95% confidence interval.

(A)

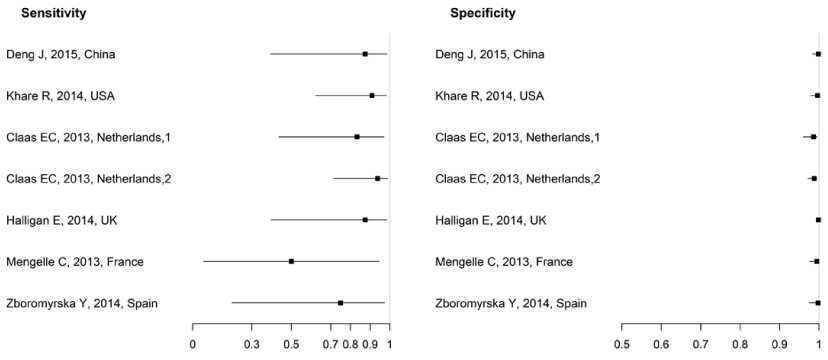
Campylobacter



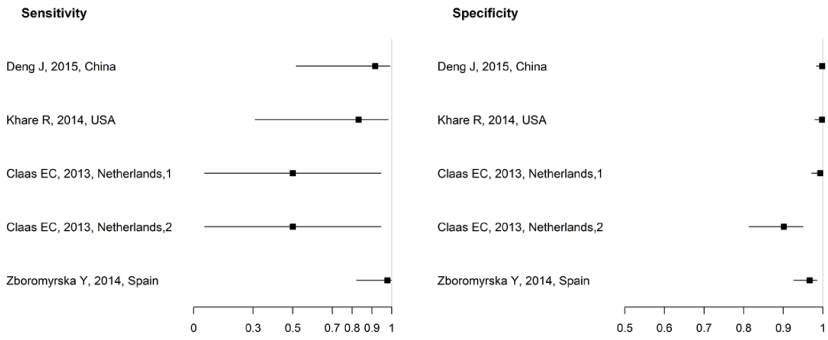

*Clostridium difficile*



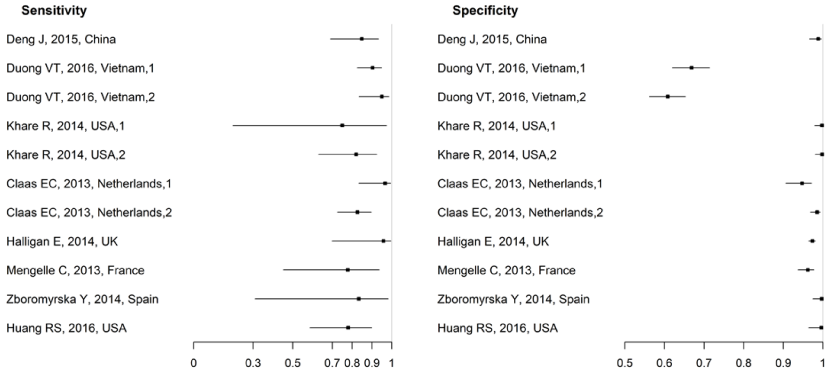

E. coli O157



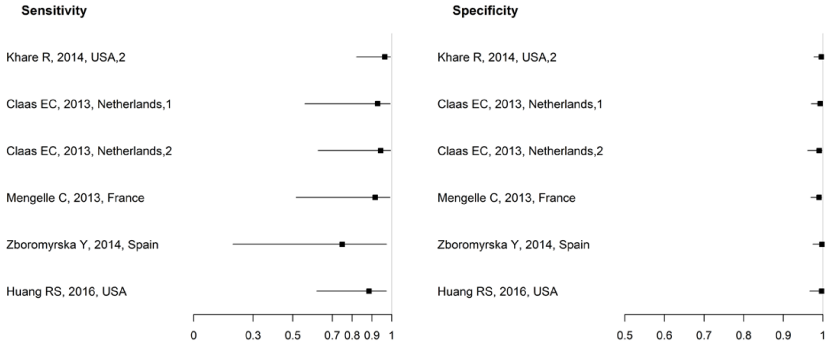
ETEC



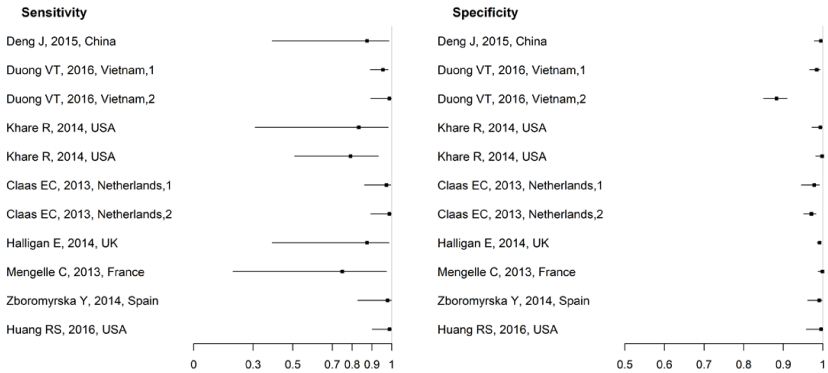

Salmonella



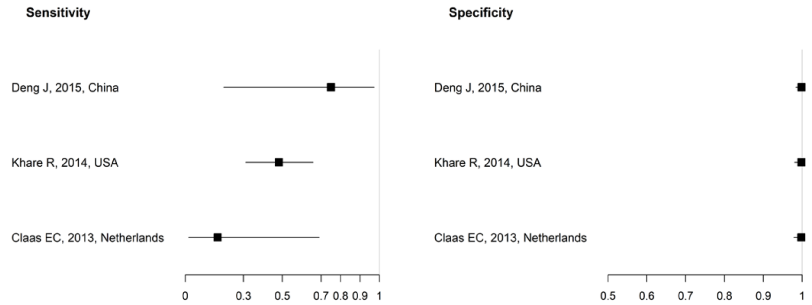

STEC stx1/stx2



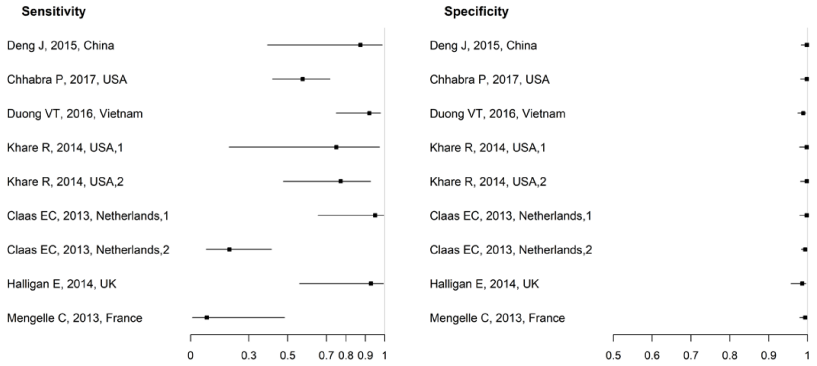

Shigella



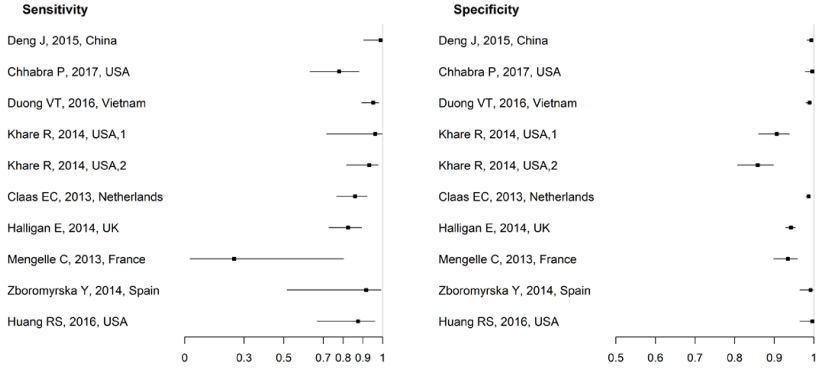
*Yersinia enterocolitica*



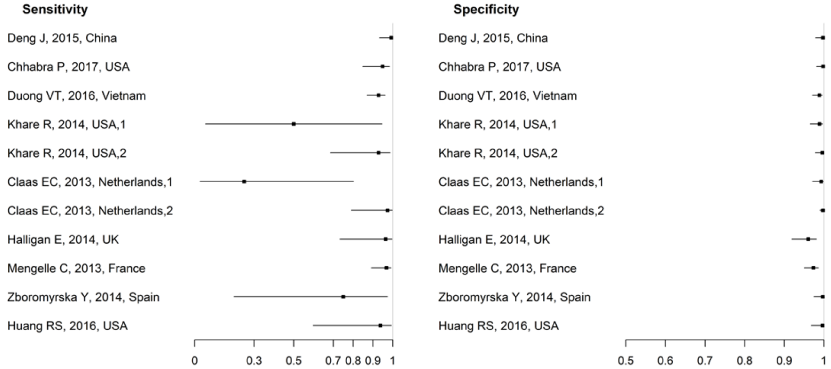

Adenovirus 40/41



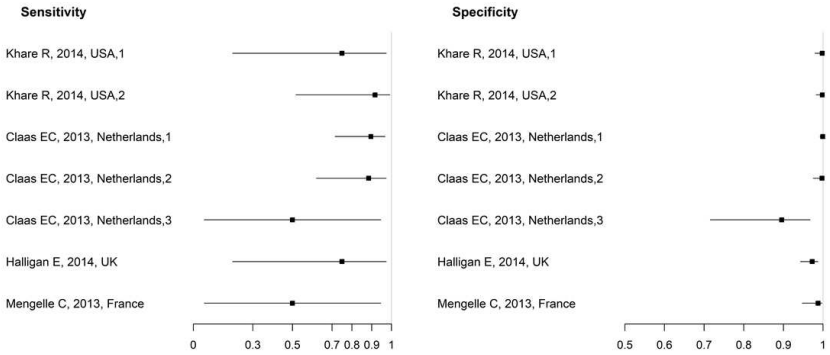

Norovirus GI/GII



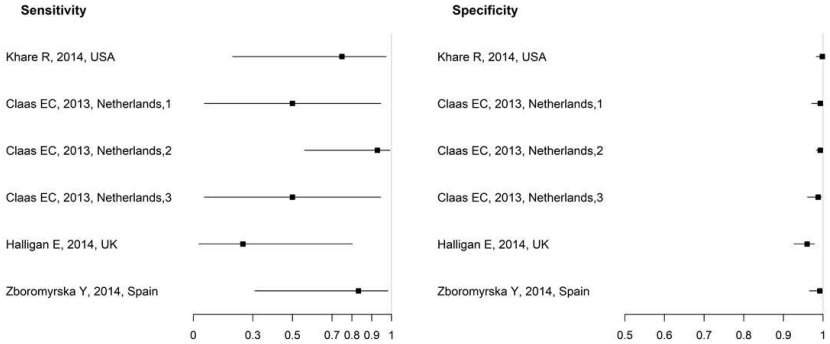

Rotavirus



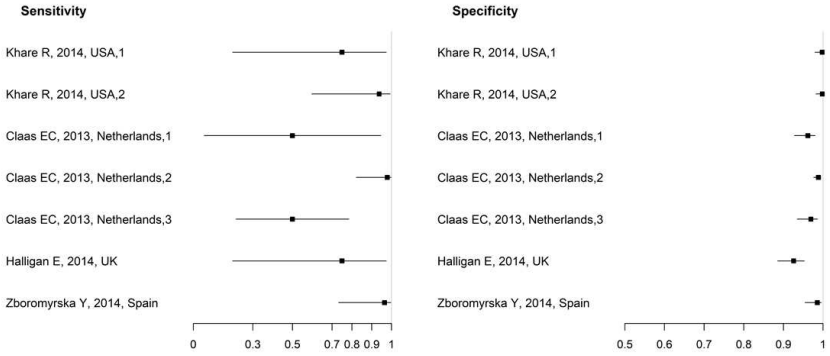
Cryptosporidium




*Entamoeba histolytica*

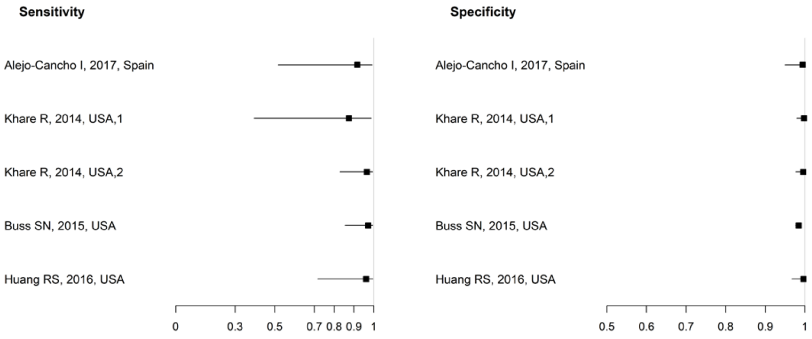



*Giardia lamblia*

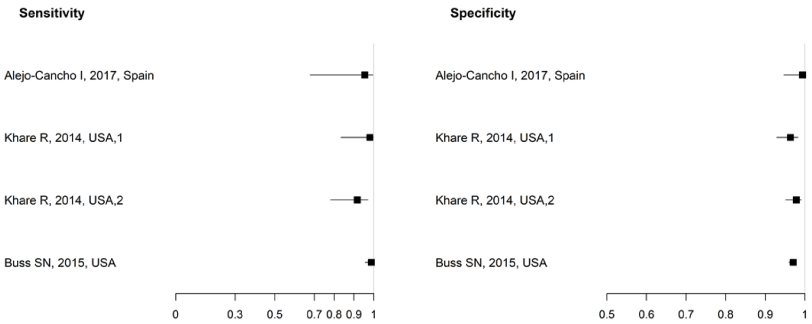


(B)

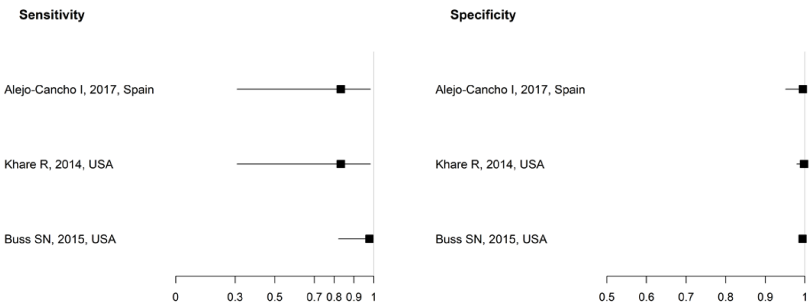
Campylobacter



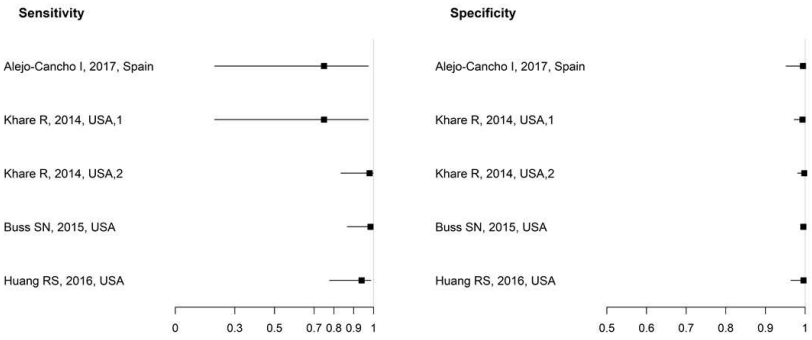

*Clostridium difficile*



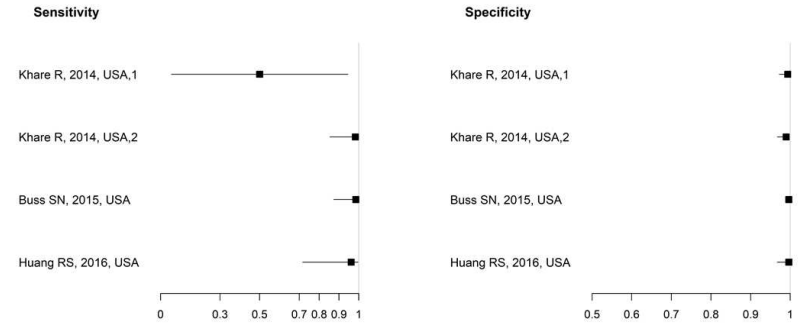

ETEC



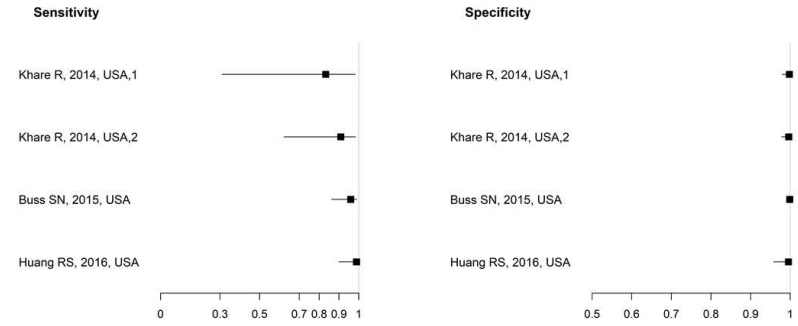
Salmonella



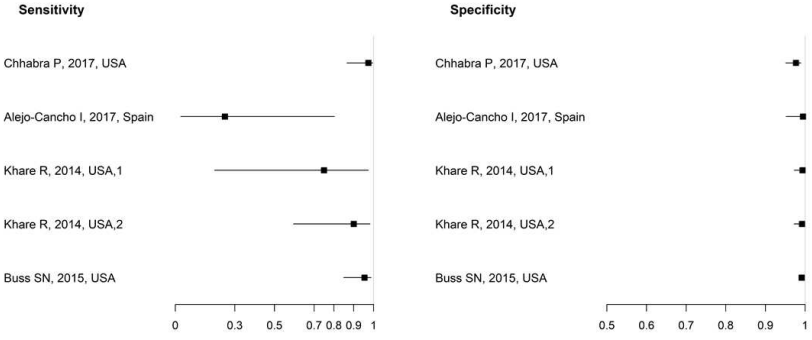

STEC stx1/stx2



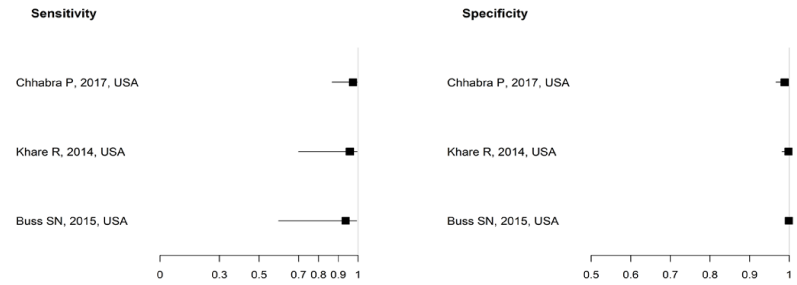

Shigella/EIEC



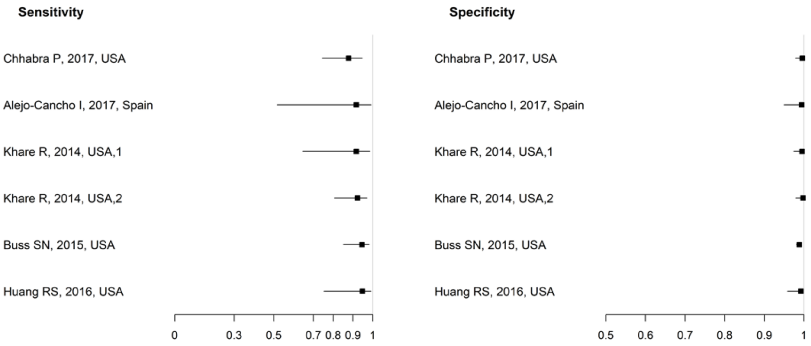

Adenovirus



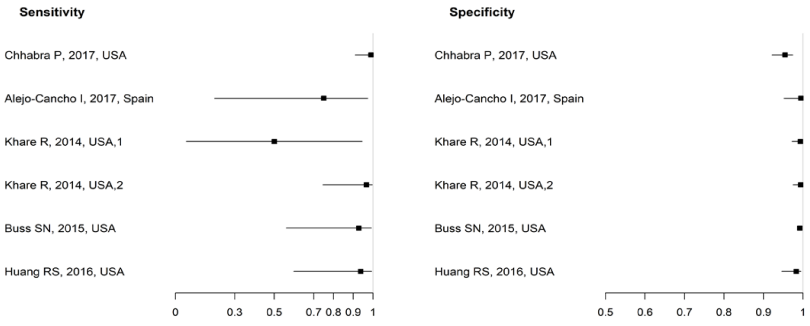
## Astrovirus



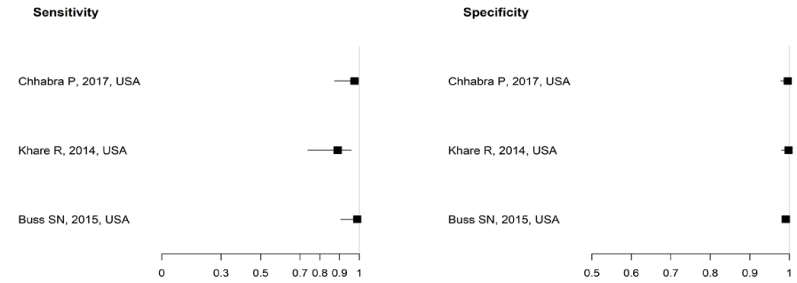

## Norovirus GI/GII

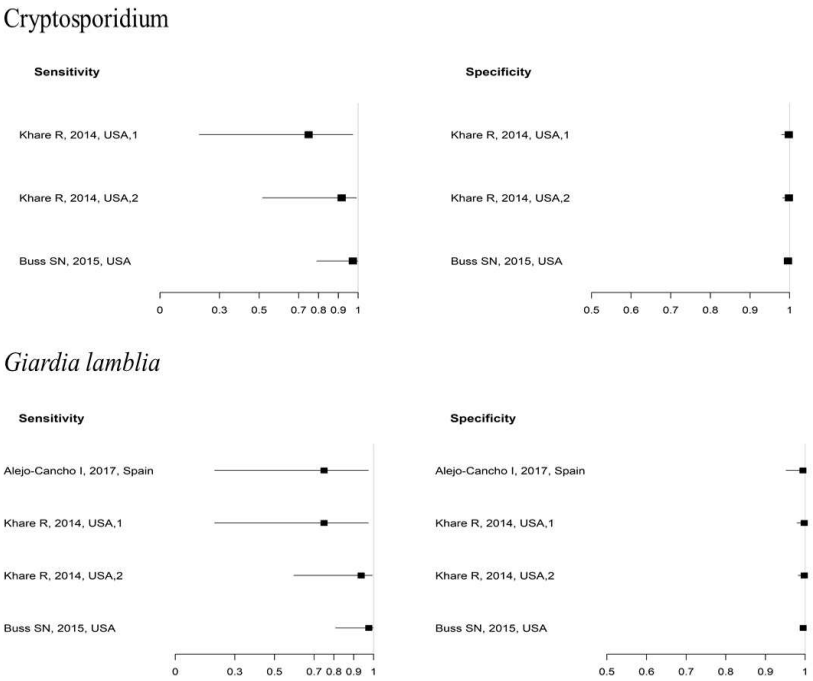



## Rotavirus

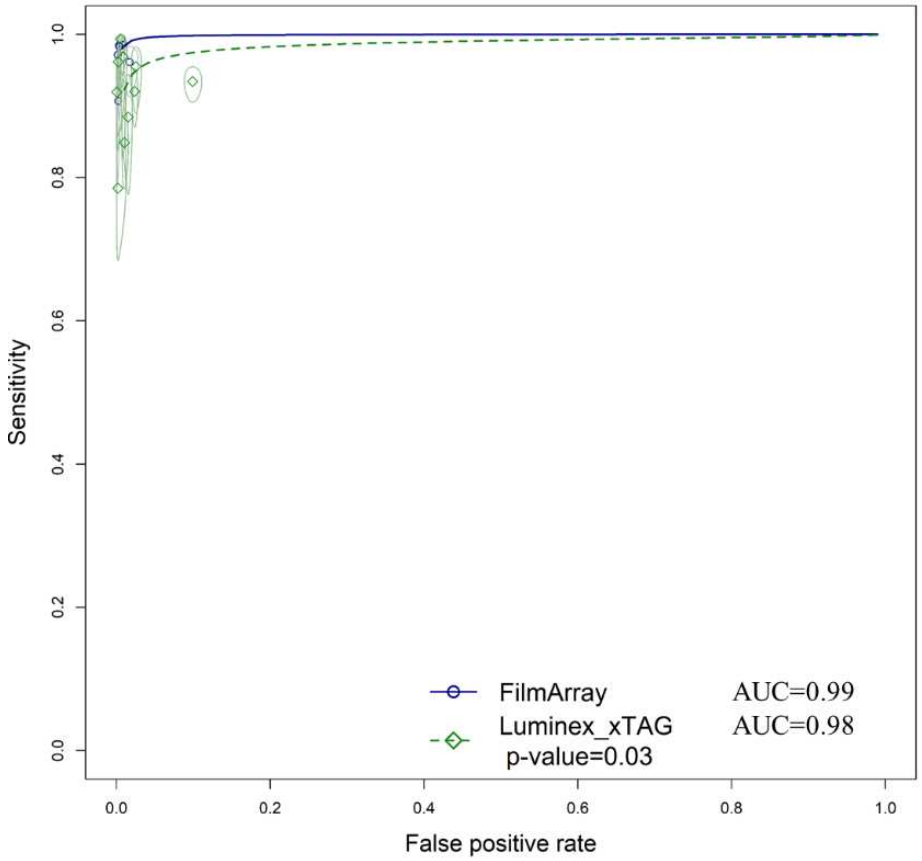



## Sapovirus






**Supplementary materials S8.** (A) Forest plot of the estimated sensitivity and specificity (black squares) of the Luminex xTAG GI panel for each pathogen, and its 95% confidence intervals (horizontal black lines) of each study. (B) Forest plot of the estimated sensitivity and specificity (black squares) of the FilmArray GI panel for each pathogen, and its 95% confidence intervals (horizontal black lines) of each study.




**Supplementary materials S9**. Summary receiver operating characteristic (SROC) curve. Dots and diamonds represent estimates of individual studies for FilmArray and Luminex, respectively. Circles represent the 95% confidence interval. SROC curves are the lines passing through summary points.

**Supplementary material S10.** Subgroup analysis for GI panel sensitivity and specificity when tested with different gold standards.

| Test | Studies number | Sensitivity (95% confidence interval) | Specificity (95% confidence interval) | AUC (95% confidence interval) | P value (compared with overall data) |
|---|---|---|---|---|---|
| **Campylobacter** | | | | | |
| Culture | 4 | 0.96(0.89-0.98) | 0.96(0.93-0.97) | 0.99(0.96-1.00) | 0.901 |
| PCR/sequencing | 2 | NA | NA | NA | NA |
| Culture and PCR/sequencing | 5 | 0.84(0.73-0.92) | 1.00(0.99-1.00) | 0.99(0.97-1.00) | 0.631 |
| Overall(Culture or PCR/sequencing) | 11 | 0.92(0.86-0.96) | 0.98(0.95-0.99) | 0.99(0.98-1.00) | ref |
| **Shigella** | | | | | |
| Culture | 4 | 0.95(0.72-0.99) | 0.98(0.91-1.00) | 0.99(0.95-1.00) | 0.942 |
| PCR/sequencing | 2 | NA | NA | NA | NA |
| Culture and PCR/sequencing | 5 | 0.92(0.75-0.98) | 0.99(0.99-1.00) | 1.00(0.98-1.00) | 0.865 |
| Overall(Culture or PCR/sequencing) | 11 | 0.95(0.88-0.98) | 0.99(0.97-0.99) | 1.00(0.99-1.00) | ref |
| **Rotavirus A** | | | | | |
| Virus antigen detection | 5 | 0.93(0.80-0.98) | 0.98(0.96-0.99) | 0.99(0.94-1.00) | 0.956 |
| PCR/sequencing | 4 | 0.93(0.88-0.96) | 0.99(0.96-0.99) | 0.99(0.98-1.00) | 0.550 |
| Virus antigen detection and PCR/sequencing | 2 | NA | NA | NA | NA |

| | | | | | |
|---|---|---|---|---|---|
| Overall (Virus antigen detection or PCR/sequencing) | 11 | 0.93(0.90-0.96) | 0.99(0.98-1.00) | 0.99(0.99-1.00) | ref |