Brendish et al. conducted a first of its kind large-scale randomized controlled trial to evaluate the clinical impact of syndromic molecular point-of-care testing (mPCOT) for gastrointestinal pathogens in adults hospitalized with suspected gastroenteritis. An increasing number of pathogens have been identified to be the causative agents of diarrhea. Most of the times, diarrhea is self-limiting and manageable with fluid therapy, whereas the severe episodes can be life threatening and require optimal antimicrobial therapy that varies with the specific causative pathogen. The diagnosis of diarrheal pathogens has always been cumbersome and problematic by conventional approaches. Patients with diarrhea are typically placed in isolation in single occupancy rooms to prevent transmission of infectious pathogens to other patients as well healthcare staff. The National Health Services in United Kingdom has approximately 40,000 of these single occupancy rooms out of a total of 111,000 acute hospital beds, with only around 1,700 designated for isolation. Above-mentioned study was conducted during the coronavirus disease 2019 pandemic, causing further diagnostic delays and strained healthcare resources for patients with diarrhea seeking hospital admission and care. Authors studied 278 adult patients of diarrhea over a period of 3 years who were randomly assigned to either mPCOT \((n=137)\) group or routine clinical care group \((n=140)\). Patients admitted to the hospital with suspected gastroenteritis were recruited to study the clinical implications on various outcomes including utilization of a single occupancy room turn-around time of tests, time to de-isolation, antibiotic administration, and safety outcomes. Acute diarrheal illness was defined as three or more stools for at least 1 day. Inclusion criteria included patients who had acute diarrhea or vomiting for up to 14 days, were at least 18 years old, and could provide written consent. Recruitment occurred within 48 hours of first triage in an emergency or 48 hours of community admission to the acute medicine and surgical unit or inpatient ward. Patients allocated to the intervention group had a stool sample or rectal swab obtained and analyzed immediately by Film-Array Gastrointestinal Panel (BioFire Diagnostics, bioMérieux, Salt Lake City, Utah, United States). Patients who were randomly assigned to receive routine clinical care (i.e., control group) had stool testing done by standard laboratory testing at the discretion of the clinical team.

In the mPCOT group, patients spent 1.8 days (95% confidence interval: 1.5–2.2) in a single occupancy room compared with 2.6 days (2.2–3.0) in the control group, signifying a 30% reduction \((p=0.0017)\). This reduction remained sig-
significant when considering multiple factors. Patients without detected pathogens in the mPCOT group had a shorter stay (1.3 days 1.0–1.6), while no difference was noted in hospital stay duration between groups for patients with detected pathogens (2.8 days in mPCOT vs. 2.9 days in control, \( p = 0.76 \)). Time-to-event analysis revealed quicker desislation after mPCOT, driven by patients in the mPCOT group with no detected pathogen. The median time for clinicians to access results was 1.7 hours in the mPCOT group versus 44.7 hours in the control group (\( p = 0.0001 \)). More patients in the mPCOT group moved from single occupancy to shared bay areas during hospitalization. More pathogens were detected in the mPCOT group (45 vs. 26%, \( p = 0.0007 \)), with Campylobacter species being the most common. Patients in the mPCOT received more antibiotics (65 vs. 47%, \( p = 0.0028 \)), particularly with a final diagnosis of gastroenteritis. Although inappropriate antibiotic use was similar, the mPCOT group resulted in shorter durations of such antibiotics nearly by 4 days. This demonstrated that the clinicians who acted upon mPCOT results either shifted to appropriate antibiotics based on the detected pathogens or discontinued antibiotics. It highlights the potency of mPCOT as an antibiotic stewardship intervention. Implementing this strategy may further enhance clinical benefits and enable more targeted therapy. Concordance between rectal swabs and stool samples for pathogen detection was high with a negative predictive value of 91%. There was a notable use of higher antibiotics in mPCOT group as compared with the control group that raises concerns about the potential overtreatment of colonizing organisms like Clostridioides difficile. However, the study reveals that the use was primarily driven by a larger proportion of patients with gastroenteritis receiving antibiotics, particularly for those with Campylobacter and enteropathogenic Escherichia coli, not Clostridioides difficile.

A prior small-scale study in the emergency department showed improved pathogen-directed antibiotic use with mPCOT but did not assess its impact on infection control measures. In contrast, a randomized controlled trial with laboratory-based molecular testing in hospitalized adults, which enrolled approximately half the number of patients as this study, found no difference in isolation facility utilization or other clinical outcomes. Another trial done in Botswana involving children using a test-and-treat strategy with rapid molecular testing did not yield improved outcomes, although the study was significantly underpowered.

In this study, the absence of differences in hospital stays length and other clinical measures between groups that factors such as age and comorbidities may be more influential determinants. Roughly a quarter of participants had inflammatory bowel disease (IBD), prompting further research into mPCOT use in IBD rapid access clinics, including outcomes related to admission avoidance, antibiotic use, and steroid treatment. Pathogen detection using rectal swabs and stool samples on the Film-Array platform showed high concordance supporting the use of routine rectal swabs to speed up diagnosis because it reduces the wait time needed for the patient to produce a stool sample and it was in concordance with previously reported studies. Patients in the mPCOT group had higher detection rates due to factors like broader testing, while the control group had missed detections, especially of Norovirus and Campylobacter spp.

Several new molecular gastrointestinal diagnostic tests based on multiplex polymerase chain reaction (PCR) panels are commercially available as demonstrated in Table 1; these detect a broad range of pathogens as compared with conventional tests. An important question is how clinicians should approach these newer diagnostics? However, cost of these newer tests is a hinderance to their cost-effectiveness in mild diarrhea episodes that are self-limiting in nature and manageable with fluid therapy. However, specific diagnosis makes the test expenses worthy for hospitalized patients especially where isolation of patient is required and which increases the expenses of hospital stays in developed countries. There is an urgent unmet need for the development of new diagnostic tests of high sensitivity and specificity similar to multiplex molecular tests but with lower costs owing to high burden of diarrhea in low middle-income countries where resources are limited. As an alternative, in-house multiplex PCR tests can be easily developed for broader identification of various diarrheal pathogens by targeting specific conserved virulence markers of various pathogens.

### Table 1 Comparison of FDA cleared multiplex panels for GI pathogens

<table>
<thead>
<tr>
<th>Sl no.</th>
<th>POC test</th>
<th>Number of targets</th>
<th>Advantages and disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FilmArray GI (bioMérieux)</td>
<td>22</td>
<td>Fully integrated system, less chances of contamination, includes viral, bacterial, and protozoal targets, run time is 1-hour, high cost</td>
</tr>
<tr>
<td>2</td>
<td>Verigene EP (Luminex)</td>
<td>9</td>
<td>Sensitivity and specificity low, parasites not detected, include viral and bacterial targets, run time is 2 hours</td>
</tr>
<tr>
<td>3</td>
<td>xTAG GPP (Luminex)</td>
<td>14</td>
<td>Not integrated system, increased chances of cross-contamination, includes viral, bacterial, and protozoal targets, batch processing, separate extraction, run time is 5 hours</td>
</tr>
<tr>
<td>4</td>
<td>Allplex GI panel (Seegene)</td>
<td>25</td>
<td>Four different multiplex PCR panels includes bacterial, viral and parasite targets, separate nucleic acid extraction, run time is 2 hours</td>
</tr>
</tbody>
</table>

Abbreviations: FDA, Food and Drug Administration; GI, gastrointestinal; PCR, polymerase chain reaction; POC, Point of Care.
Ethical Statement
Not applicable.

Author Contribution
All authors contributed equally to the article.

Data Availability Statement
There is no data associated with this work.

Funding
None.

Conflict of Interest
None.

Acknowledgments
None.

References