Open Forum Infectious Diseases

BRIEF REPORT

Prevalence of Gastrointestinal Pathogens Detected by Multiplex Polymerase Chain Reaction in a Prospective Cohort of Men Who Have Sex With Men Taking Human Immunodeficiency Virus Preexposure Prophylaxis—New York City, 2019–2020

Lawrence Purpura,[1,2] Jason Zucker,[1] Elijah LaSota,[1] Mabel Lopez,[3] Rebecca Spicehandler,[1] Caroline Carnevale,[4] Edward Perez,[4] Paul Richards,[4] Jennifer Chang,[1] Al Cohall,[4] Anne-Catrin Uhlemann,[1] Susan Whittier,[3] Magdalena E. Sobieszczyk,[1] and Daniel A. Green[3]

[1]Division of Infectious Diseases, Department of Medicine, Columbia University Irving Medical Center, New York, New York, USA, [2]ICAP, Mailman School of Public Health, Columbia University, New York, New York, USA, [3]Clinical Microbiology, Department of Pathology, Columbia University Irving Medical Center, New York, New York, USA, and [4]New York Presbyterian–Columbia Hospital, New York, New York, USA

Multiplex polymerase chain reaction testing for gastrointestinal pathogens was performed on a longitudinal cohort of 110 men who have sex with men taking human immunodeficiency virus preexposure prophylaxis. At least 1 pathogen was detected among 50 (45%) participants, with some participants testing positive for the same pathogen on multiple consecutive visits over a period of months.

Keywords. gastrointestinal pathogen; men who have sex with men; polymerase chain reaction; preexposure prophylaxis.

Sexual transmission of gastrointestinal (GI) pathogens is both a historical and emerging phenomenon among men who have sex with men (MSM), with outbreaks of *Shigella* and *Campylobacter* reported with increasing frequency [1, 2] worldwide. In addition to gastroenteritis, these pathogens can also cause proctitis or proctocolitis, yet current management of rectal symptoms for MSM is empiric treatment for gonorrhea and chlamydia [3] only, and testing for GI pathogens is currently only performed in the setting of diarrhea. In the context of these practices, the burden of antibiotic resistance is increasing in *Shigella* [4–6] and *Campylobacter* [2].

Outside of outbreak investigations, the prevalence of enteric pathogens in MSM is not well characterized. Among symptomatic MSM with gastroenteritis in the US state of Washington, *Escherichia coli*, *Shigella*, *Campylobacter*, *Norovirus*, and *Giardia* were most frequently identified [7]. Only 1 study, in Melbourne, Australia, has described asymptomatic carriage of pathogenic enteric organisms in MSM, with a cross-sectional prevalence of 11% [8]. To date, prospective data regarding prevalence and symptomatology are lacking. Here we present the prevalence of GI pathogens and correlation with clinical factors in a prospective cohort of MSM receiving preexposure prophylaxis (PrEP) for HIV in New York City.

METHODS

Patient Population

This study was performed at a sexual health clinic within a large urban academic medical center in northern Manhattan. Adult HIV-negative MSM were recruited from a prospective PrEP adherence study (Stick2PrEP) from 7 February 2019 until 12 March 2020, and the enrolled population reflects the overall clinic population [9].

Study Design

At regular 3-month clinic visits for PrEP follow-up, regardless of symptoms, an additional flocculated rectal swab placed in Carey-Blair transport media (FecalSwab, Copan Diagnostics, Murietta, California) was collected at the same time as a clinical rectal swab for gonorrhea and chlamydia testing; the additional rectal swabs were tested for 22 organisms by multiplex polymerase chain reaction (PCR) off-label with the FilmArray GI Panel (BioFire Diagnostics, Salt Lake City, Utah) [10]. GI Pathogen PCR results were used for research purposes only and not made available to patients or their providers. Participants completed an enrollment survey describing demographics and sexual risk factors, and at each visit a survey on GI symptoms and potential exposures. Study follow-up was 12 months but ended early for the majority due to the coronavirus disease 2019 (COVID-19) pandemic.

Data Analysis

Demographics, clinical variables, and pathogen species were assessed using descriptive statistics. Associations with a positive swab, clinical outcomes, and sexual health behavior were assessed using χ^2 for categorical and Student *t* test for continuous variables. A P value <.05 was considered significant. Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, North Carolina).

Received 13 May 2021; editorial decision 28 July 2021; accepted 2 August 2021.

Correspondence: Daniel A. Green, MD, New York–Presbyterian/Columbia University Medical Center, 622 W 168th St, New York, NY 10032, USA (dag2149@cumc.columbia.edu).

Open Forum Infectious Diseases®2021

https://doi.org/10.1093/ofid/ofab411

Ethics Statement

This study was approved by the Columbia University Irving Medical Center Institutional Review Board.

RESULTS

From 7 February 2019 to 12 March 2020, 110 of 148 (74%) participants in Stick2PrEP study enrolled in the GI pathogen substudy. Overall, 98% identified as male and 45% as Hispanic. Thirty-five percent reported income <$20 000 per year, 45% did not have a college degree or higher, and 45% reported not having health insurance (Supplementary Table 1).

A total of 194 rectal swabs were collected from 110 participants. More than 1 study visit was completed by 50 (45%) participants, with 22 (20%) completing 3 visits, 11 (10%) completing 4 visits, and 1 (1%) completing 5 visits. Median number of days between study visits was 98 (range, 12–315). At least 1 organism was detected in 62 (32%) rectal swabs from 50 (45%) participants; 1 swab was invalid and excluded from the analysis. Enteropathogenic *E coli* (EPEC) was detected in 20 (10%) rectal swabs, *Giardia lamblia* in 19 (10%), enteroaggregative *E coli* (EAEC) in 16 (8%), *Campylobacter* in 14 (7%), *Shigella*/enteroinvasive *E coli* in 4 (2%), enterotoxigenic *E coli* in 1 (<1%), *Vibrio* in 2 (1%), *Cryptosporidium* in 2 (1%), *Norovirus* in 2 (1%), and *Sapovirus* in 1 (<1%) (Figure 1, Supplementary Table 2). *Giardia* was detected in 3 consecutive swabs in 2 participants and 2 consecutive swabs in 1 participant. *Campylobacter* was detected on 3 consecutive swabs in 1 participant and 2 consecutive swabs in 1 additional participant. EPEC was detected on 3 consecutive swabs in 1 participant and EAEC on 2 consecutive swabs in 1 participant. The median number of days between visits was 91 (range, 28–119) for 2 consecutive positive swabs and 91 (range, 63–119) for a positive swab followed by a negative swab. More than 1 organism was detected in 16 rectal swabs, with 4 organisms detected in 1 swab, 3 in 2 swabs, and 2 in 13 swabs.

Symptoms reported within 30 days of rectal swab collection are reported in Supplementary Table 3. Overall, frequency of symptoms was high irrespective of swab results; 41 of 62 (66%) positive and 81 of 130 (62%) negative rectal swabs were associated with ≥1 symptom. The most commonly reported symptoms were diarrhea (43%), abdominal discomfort (32%), urgency (27%), tenesmus (18%), nausea (18%), and mucus in stool (10%). There was no significant difference in reporting of associated symptoms or self-reported antibiotic use with PCR results. At least 1 symptom was associated with most pathogens; however, only 60% of EPEC, 63% of EAEC, 50% of *Shigella*, 64% of *Campylobacter*, and 74% of *Giardia* positive swabs were associated with at least 1 symptom.

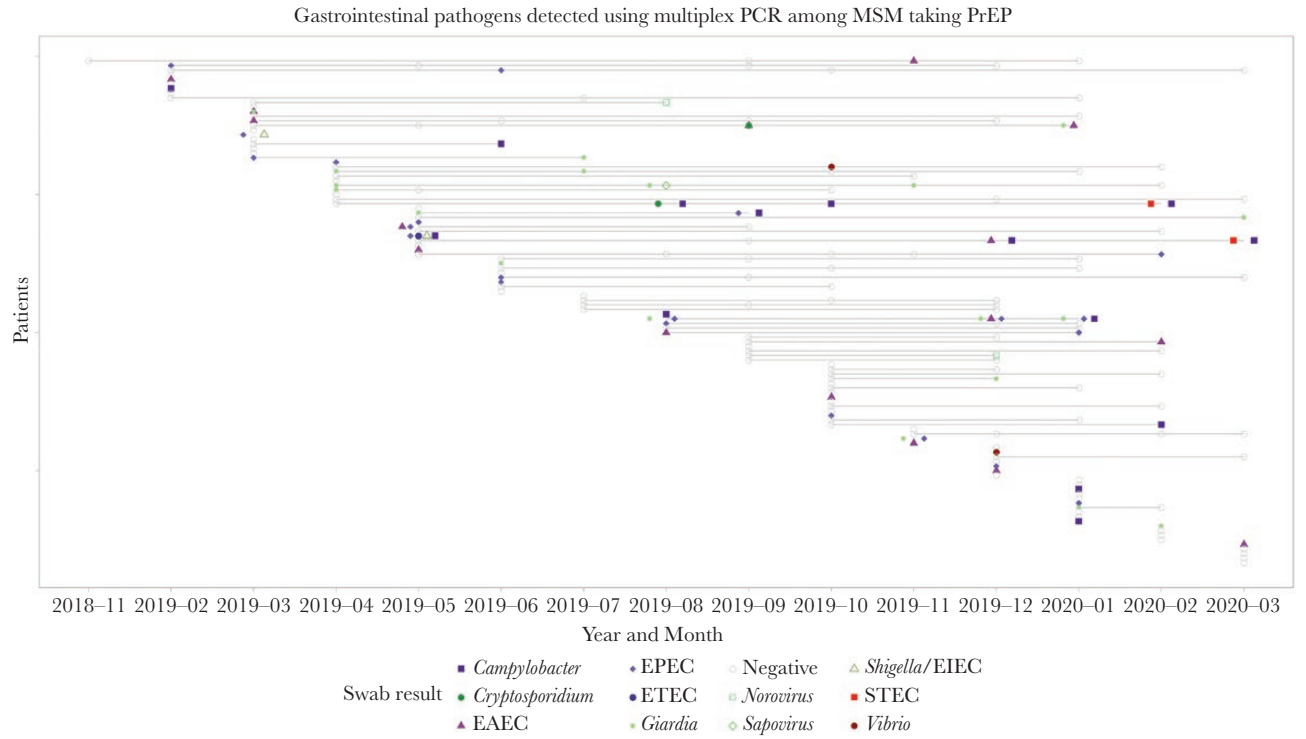

Figure 1. Longitudinal multiplex polymerase chain reaction results of rectal swabs from men who have sex with men receiving human immunodeficiency virus preexposure prophylaxis. Abbreviations: EAEC, enteroaggregative *Escherichia coli*; EIEC, enteroinvasive *Escherichia coli*; EPEC, enteropathogenic *Escherichia coli*; ETEC, enterotoxigenic *Escherichia coli*; MSM, men who have sex with men; PCR, polymerase chain reaction; PrEP, preexposure prophylaxis; STEC, Shiga toxin–producing *Escherichia coli*.

Risk factors associated with acquiring a GI pathogen are displayed in Supplementary Tables 4 and 5. PCR results were not significantly associated with travel, sick contacts, or reported sexually transmitted infection in the preceding 30 days. There was a trend toward less frequent condom use associated with positive swabs compared to negative swabs (4.4 compared to 5.4 condom use out of 10 sex encounters, respectively; $P = .06$). Although there was no difference in number of sexual partners in the preceding 30 days or perceived sexually transmitted infection risk reported at baseline, a negative swab result was associated with higher, but not statistically significant, number of receptive anal sex encounters in the past 6 months (8.58 vs 5.25; $P = .07$).

DISCUSSION

To our knowledge, this is the largest longitudinal study to date of enteric pathogen prevalence among MSM attending a sexual health clinic. We observed a surprisingly high detection rate, with 45% of participants having at least 1 positive swab during the study period and 32% of all swabs detecting at least 1 pathogen. Multiple pathogens were detected in 16 of 62 (26%) of swabs. The same pathogen was detected on consecutive swabs from 9 (8%) participants, suggesting long-term carriage. Overall, GI symptoms were common but not significantly associated with PCR results, with 44% of positive swabs not associated with any symptom.

Notably, the distribution of pathogens among MSM in our study differed substantially from the baseline distribution of GI pathogens among all 9402 patients with diarrhea who underwent FilmArray GI Panel testing at our medical center from 2015 to 2017 [11]. Whereas *E coli* subtypes and viruses accounted for 52% and 39% of all positive tests, respectively, among the general population, they accounted for 60% and 5% of positive tests among MSM in our study. In addition, *Giardia* was identified much more frequently among MSM (10% vs 1.3%).

While giardiasis has been well-described among HIV-positive MSM [12], its prevalence among HIV-negative MSM is not as well understood. In a prospective study of 253 MSM presenting with acute gastroenteritis in Seattle, Washington, *Giardia* accounted for 14% of positive stool specimens among HIV-positive MSM and 33% of positive stool specimens among HIV-negative MSM [7]. Our study lends further support to the high prevalence of *Giardia* in the HIV-negative MSM population, and furthermore, provides evidence of long-term carriage. While EPEC, EAEC, and *Campylobacter* were frequently detected in both studies, *Shigella* and viral etiologies (particularly *Norovirus*), were seen much more frequently among the symptomatic Seattle cohort, suggesting asymptomatic carriage of these pathogens is less common.

The prospective nature of our study allowed us to study long-term carriage. In total, 9 participants had a positive swab at >1 consecutive visit. *Giardia* or *Campylobacter* were identified at up to 3 consecutive visits in 5 participants and these swabs were not always associated with gastrointestinal symptoms. These findings have important implications regarding asymptomatic carriage and potential transmission risk to sexual partners; however, further research is needed to definitively evaluate true carriage vs reinfection.

Our study is subject to several limitations. First, participants were recruited from a single academic center and the study was restricted to MSM who were enrolled in a cell phone–based PrEP adherence study, so our results may not be generalizable to the general MSM population. Second, due to the COVID-19 pandemic, our overall sample size was limited and only 46% of participants completed >1 study visit, limiting our ability to assess incidence of pathogen detection and longitudinal carriage. Third, the FilmArray GI Panel is not US Food and Drug Administration approved for use with rectal swabs, although the performance of flocculated rectal swabs has been previously shown not to differ from stool [13]. Fourth, sexual health questions were asked at enrollment and may not represent behavior at the time of swab collection. Last, antimicrobial resistance data were not obtained but would be important to assess from a public health perspective, particularly for *Shigella* and *Campylobacter*.

CONCLUSIONS

Overall, we found a high rate of enteric pathogen detection among HIV-negative MSM taking PrEP, with 45% of participants having at least 1 positive rectal swab during the study period, most commonly with EPEC, EAEC, *Campylobacter*, and *Giardia*. GI symptoms were common among all participants, but not significantly associated with positive PCR results and may not be useful as screening stratification. While the clinical relevance of EPEC and EAEC is less clear, *Campylobacter* and *Giardia* are both associated with sexual transmission among MSM, and the high rate of detection we observed may have important public health implications. Testing of partners within a sexual network would be needed, however, to assess true transmission risk and community spread. Importantly, *Giardia* is not covered by current empiric treatment for proctitis or lymphogranuloma venereum. Furthermore, emerging antimicrobial resistance of *Shigella* and *Campylobacter* is a significant concern, and empiric treatment may further select resistant isolates. Given these concerns, sexual health testing strategies should consider the use of multiplex PCR screening for GI pathogens in MSM with GI symptoms, and asymptomatic screening may be beneficial in high-prevalence or outbreak settings.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility

of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. The authors would like to thank Brianne Couturier, Beth Lingenfelter, Christine Ginocchio, Matt Schaffer, and Cameron Kapp for their support.

Patient consent statement. This study was approved by the Columbia University Irving Medical Center Institutional Review Board. Written informed consent was obtained from each participant.

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health (NIH) or BioFire Diagnostics.

Financial support. This study was supported in part by funding from BioFire Diagnostics under an investigator-initiated grant (to D. A. G.). L. P. was supported by the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH (award number T32AI114398). J. Z., E. L. S., M. E. S., and J. C. were supported by the NIAID (award number UM1AI069470) and the HIV Vaccine Trials Network Initiatives Program (award number NIAID 2UM1AI068614-09 to M. E. S.).

Potential conflicts of interest. D. A. G. received research funding from BioFire Diagnostics. All other authors: No reported conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Greninger AL, Addetia A, Starr K, et al. International spread of multidrug-resistant *Campylobacter coli* in men who have sex with men in Washington State and Québec, 2015-2018. Clin Infect Dis **2020**; 71:1896–904.
2. Mitchell HD, Mikhail AFW, Painset A, et al. Use of whole-genome sequencing to identify clusters of *Shigella flexneri* associated with sexual transmission in men who have sex with men in England: a validation study using linked behavioural data. Microb Genomics **2019**; 5:e000311.
3. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines. **2015**. https://www.cdc.gov/std/tg2015/proctitis.htm. Accessed 7 July 2021.
4. Bowen A, Grass J, Bicknese A, et al. Elevated risk for antimicrobial drug-resistant *Shigella* infection among men who have sex with men, United States, 2011-2015. Emerg Infect Dis **2016**; 22:1613–6.
5. Ingle DJ, Easton M, Valcanis M, et al. Co-circulation of multidrug-resistant *Shigella* among men who have sex with men in Australia. Clin Infect Dis **2019**; 69:1535–44.
6. Mook P, McCormick J, Bains M, et al. ESBL-producing and macrolide-resistant *Shigella sonnei* infections among men who have sex with men, England, 2015. Emerg Infect Dis **2016**; 22:1948–52.
7. Newman KL, Newman GS, Cybulski RJ, Fang FC. Gastroenteritis in men who have sex with men in Seattle, Washington, 2017-2018. Clin Infect Dis **2020**; 71:109–15.
8. Williamson DA, Chow EPF, Lee D, et al. Risk factors for asymptomatic enteric pathogen detection among men who have sex with men. Open Forum Infect Dis **2019**; 6:ofz326.
9. Carnevale C, Zucker J, Borsa A, et al. Engaging a predominantly Latino community in HIV prevention: laying the groundwork for pre-exposure prophylaxis and HIV sexual health programs. J Assoc Nurses AIDS Care **2020**; 31:92–7.
10. BioFire. BioFire FilmArray gastrointestinal panel. https://www.biofiredx.com/products/the-filmarray-panels/filmarraygi/. Accessed 7 July 2021.
11. Axelrad JE, Freedberg DE, Whittier S, et al. Impact of gastrointestinal panel implementation on health care utilization and outcomes. J Clin Microbiol **2019**; 57:e01775-18.
12. Stark D, Barratt JL, van Hal S, et al. Clinical significance of enteric protozoa in the immunosuppressed human population. Clin Microbiol Rev **2009**; 22:634–50.
13. Walker CR, Lechiile K, Mokomane M, et al. Evaluation of anatomically designed flocked rectal swabs for use with the BioFire FilmArray gastrointestinal panel for detection of enteric pathogens in children admitted to hospital with severe gastroenteritis. J Clin Microbiol **2019**; 57:e00962-19.