Risk Factors for Asymptomatic Enteric Pathogen Detection Among Men Who Have Sex With Men

Deborah A. Williamson,1 Eric P. F. Chow,2 Darren Lee,1 Kate Maddaford,2 Michelle Sait,1 Marion Easton,4 Danielle Ingle,1 Rebecca Wigan,2 Vesna De Petra,1 Benjamin P. Howden,1 Christopher K. Fairley,2,3 and Marcus Y. Chen2,3

1Microbiological Diagnostic Unit Public Health Laboratory, Department of Microbiology and Immunology, The University of Melbourne at The Peter Doherty Institute for Infection and Immunity, Australia; 2Melbourne Sexual Health Centre, Alfred Health, Carlton, Victoria, Australia; 3Central Clinical School, Monash University, Melbourne, Australia; 4Victorian Department of Health and Human Services, Melbourne, Australia

Improved knowledge of factors that promote outbreaks of enteric pathogens among men who have sex with men (MSM) could enable targeted public health interventions. We detected enteric pathogens in 57 of 519 (11%) asymptomatic MSM, and we found that enteric pathogen detection was associated with both oroanal sex (rimming) and group sex.

Keywords. enteric pathogens; epidemiology; gastrointestinal disease; sexually transmitted infections.

Gastrointestinal infections are a major global cause of morbidity. Transmission of enteric pathogens occurs predominantly by the fecal-oral route, through ingestion of contaminated food or water. Sexual transmission is also a well recognized mode of transmission, mainly amongst men who have sex with men (MSM), and, over the past decade, there have been increasing reports of outbreaks of enteric pathogens among MSM, including Shigella spp, Shiga-toxin-producing Escherichia coli (STEC), and hepatitis A virus [1–7]. In particular, sexually transmitted shigellosis has emerged as a major public health concern, mainly due to high rates of resistance to clinically relevant antimicrobials [4, 5, 8]. In our setting, we recently described the cocirculation of 2 major drug-resistant Shigella lineages among MSM over a 27-month period, with each lineage including at least 50 men [5]. To date, however, the biological and behavioral factors that drive the persistence of shigellosis epidemics in MSM are not well defined.

Given the extent and persistence of Shigella in MSM in our setting, we hypothesised that asymptomatic carriage of enteric pathogens, including Shigella, could act as a potential reservoir for gastrointestinal outbreaks in MSM, and that improved knowledge of factors that promote outbreaks of enteric disease could enable public health interventions to be directed towards those at highest risk of disease. To address these hypotheses, we performed a cross-sectional study of asymptomatic MSM in Melbourne, Australia, and we screened for the presence of 15 bacterial, viral, and protozoan enteric pathogens. Furthermore, we examined the association between behavioral risk factors and the presence of asymptomatic enteric pathogens to better understand the drivers of sexually transmitted enteric infections in MSM.

METHODS

Setting, Patients, and Data Sources
Melbourne Sexual Health Centre is the major publicly funded sexual health center in Victoria, Australia, with approximately 50 000 consultations annually [9]. The center consists of a free walk-in sexually transmitted infections (STI) clinic and outpatient human immunodeficiency virus (HIV) and HIV pre-exposure prophylaxis (PrEP) clinics. Between November 1, 2018 and February 28, 2019, we undertook a cross-sectional study to estimate the prevalence of enteric pathogens in asymptomatic MSM (those who did not have diarrhea in the 2 weeks before testing) attending for STI screening. Recruitment focused on 3 groups of MSM: HIV-negative men currently taking PrEP, HIV-negative men not taking PrEP, and HIV-positive men. All men completed a brief questionnaire (Supplementary Appendix) that captured information on age, HIV status, use of PrEP, and diarrhea (defined as ≥3 loose or liquid stools within the last 2 weeks). Men were asked about sexual practices, including group sex in the last month, use of party drugs in the last month, and insertive rimming (mouth or tongue touching another man’s anus) within the last 12 months.

Microbiological Testing
Routine STI screening consisted of an oropharyngeal swab, first pass urine, and an anal swab for Neisseria gonorrhoeae and Chlamydia trachomatis nucleic acid amplification testing using the Aptima Combo 2 assay (Hologic). Men who agreed to the study had another anal swab collected using an ESwab (Copan Diagnostics Inc., Brescia, Italy). Deoxyribonucleic acid (DNA) was extracted using the QIASymphony DSP Virus/Pathogen Midi Kit (QIAGEN) protocol according to the manufacturer’s instructions. Extracted DNA was tested on a High-Plex24 system using the Faecal Pathogen M 16-well assay (AusDiagnostics Pty. Ltd., Sydney, Australia), a multiplexed
tandem polymerase chain reaction (PCR) assay that can detect 15 enteric pathogens (Supplementary Table 1).

Statistical Analysis
Proportions of enteric pathogens were calculated with 95% binomial confidence intervals (CIs). Associations with enteric pathogen detection were assessed using univariate and multivariable logistic regression analyses. Sexual behaviors with \( P < .10 \) in the univariable analyses were included in the multivariable model. Statistical analyses were performed in STATA (version 14.2; Stata Corporation, College Station, TX).

Ethics
Ethical approval was obtained from the Alfred Hospital Ethics Committee (Project 271/18).

RESULTS
Characteristics of Study Population and Prevalence of Enteric Pathogens
Overall, 519 MSM were included in the study, with ages ranging between 18 and 73 years (median 31 years; interquartile range 26–40 years). A total of 78 of 519 men (15.0%; 95% CI, 12.2%–18.3%) were HIV-positive, and of the remaining HIV-negative men, 227 of 441 (51.5%; 95% CI, 46.8%–56.1%) were taking PrEP. Overall, 363 of 505 MSM (71.9%; 95% CI, 67.8%–75.6%) reported insertive rimming in the last 12 months, 123 of 519 (23.7%; 95% CI, 20.2%–27.6%) reported group sex in the last month (with the number of episodes ranging from 1 to 30), and 68 of 519 (13.1%; 95% CI, 10.5%–16.3%) men reported using party drugs in the last month (with the number of episodes ranging from 1 to 20).

Prevalence and Risk Factors for Enteric Pathogen Detection
Rectal swabs from 57 of 519 (11.0%; 95% CI, 8.4%–14.0%) men tested positive for any enteric pathogen (Supplementary Table 2). The most common pathogen detected was 

![Campylobacter](https://via.placeholder.com/150)

spp (13 of 519; 2.5%; 95% CI, 1.5%–4.3%), followed by astrovirus (10 of 519; 1.9%; 95% CI, 1.0%–3.6%), 

![Yersinia](https://via.placeholder.com/150)

spp (9 of 519; 1.7%; 95% CI, 0.8%–3.3%), and Shiga-toxin-producing 

![Escherichia coli](https://via.placeholder.com/150)

(Ecoli) (9 of 519; 1.7%; 95% CI, 0.8%–3.3%) (Supplementary Table 2). 

![Shigella](https://via.placeholder.com/150)

spp were detected in 5 of 519 men (1.0%; 95% CI, 0.3%–2.3%). Two enteric pathogens were detected in 8 of 519 men (1.5%; 95% CI, 0.7%–3.1%) (Supplementary Table 2).

There was no difference in the prevalence of enteric pathogen carriage between different age groups or HIV status (Table 1). Likewise, there was no significant difference in enteric pathogen carriage between PrEP and non-PrEP users (Table 1). However, when behavioral factors were adjusted, the prevalence of enteric pathogen detection was independently associated (1) with men who reported insertive rimming (adjusted odds ratio [aOR] = 3.32; 95% CI, 1.38–7.97) and (2) with men who reported group sex (aOR = 2.00; 95% CI, 1.11–3.60) (Table 1).

Overall, a total of 85 of 519 (16.4%) individuals had concurrent gonorrhea (oropharyngeal [29 of 489; 5.9%], anorectal [18 of 486; 3.7%], urethral [6 of 492; 1.2%]) or chlamydia (oropharyngeal [7 of 493; 1.4%], anorectal [44 of 486; 9.1%], urethral [17 of 492; 3.5%]). Of note, men with anorectal chlamydia had 2.33 (95% CI, 1.025–5.16) times more odds of having an enteric pathogen detected (Table 1).

DISCUSSION
In this study, 11% of asymptomatic MSM had at least 1 viral or bacterial enteric pathogen detected, with detection associated with both insertive rimming and group sex. To our knowledge, our study represents the first to link asymptomatic enteric pathogen carriage in MSM with specific behavioral risk factors. Although sexual transmission of enteric pathogens has been recognized for several decades, as early as the 1970s when the term “gay bowel syndrome” was used [10], there remains limited understanding of the specific drivers for outbreaks of enteric infections in MSM, including the role of asymptomatic carriage in facilitating transmission.

Over a 4-month period, we detected a range of enteric pathogens, including pathogens associated with outbreaks among MSM. For example, 

![Campylobacter](https://via.placeholder.com/150)

spp, identified in 2.5% of asymptomatic MSM in our study, has previously been associated with gastrointestinal outbreaks in MSM, including an outbreak of erythromycin- and ciprofloxacin-resistant 

![Campylobacter jejuni](https://via.placeholder.com/150)

in Quebec, Canada [11], and it has previously been identified in 1.8% of MSM with confirmed rectal chlamydia [12]. Likewise, STEC, identified in 1.7% of MSM in this study, was described in an MSM-associated outbreak in the United Kingdom (UK) in 2014 [3]. Of note, genomic analysis of isolates from this UK outbreak demonstrated the presence of shared antimicrobial resistance determinants (most notably the 

![mpd](https://via.placeholder.com/150)

gene encoding azithromycin resistance) between STEC and 

![Shigella](https://via.placeholder.com/150)

spp [4]. This finding is of particular relevance in our setting, where we recently identified azithromycin resistance rates of over 90% in MSM-associated 

![Shigella](https://via.placeholder.com/150)

spp in 5 individuals (1.0%), the relatively high number of partners some MSM have places them at significant risk, even with this low prevalence. For example, the Australian National Pleasure and Sexual Health (PASH) study found that, among 1590 MSM who reported having sex with casual partners in the preceding 6 months, the median number of partners was 6, with at least 60% of the 1590 MSM engaging in rimming [13]. It is likely that frequent oroanal contact, coupled with asymptomatic carriage of a highly infectious pathogen, and fueled by selection pressure from azithromycin, are drivers of shigellosis in MSM in our setting.

Previous work has shown that direct oroanal contact (rimming) is associated with acute, symptomatic enteric infections, including shigellosis and STEC [14, 15]. Our observation that enteric pathogen carriage is independently associated with
group sex supports the potential for not only direct oroanal acquisition, but also indirect acquisition. However, we did not collect the number of insertive rimming partners, so our finding that group sex was associated with enteric pathogen detection may be confounded by the number of partners during group sex.

Our exploratory study had a number of limitations, and it raised several important questions for future work. First, our study was conducted at a single sexual health service in Australia and may not be generalizable to all MSM. Second, we did not collect detailed epidemiological data to allow us to adjust for all possible risk factors such as occupational exposure (eg, to animals or childcare), contact with an affected individual, or individual hygiene habits. However, our observation of an association between detection of an enteric

### Table 1. Associations Between Men Who Have Sex With Men and Enteric Pathogen Detection

| Characteristics                          | Detection of an Enteric Pathogen, n/N (%) | OR (95% CI) | PValue | Adjusted OR (95% CI) | PValue |
|------------------------------------------|------------------------------------------|-------------|--------|----------------------|--------|
| Age (Years)                              |                                          |             |        |                      |        |
| 18–24                                    | 9/84 (10.7%)                             | 1 (ref)     |        |                      |        |
| 25–34                                    | 29/240 (12.1%)                           | 1.15 (0.52–2.53) | .737  |                      |        |
| ≥35                                      | 19/195 (9.7%)                            | 0.90 (0.39–2.08) | .805  |                      |        |
| HIV and PrEP Status                      |                                          |             |        |                      |        |
| HIV negative, no PrEP                    | 20/214 (9.3%)                            | 1 (ref)     |        |                      |        |
| HIV negative, on PrEP                    | 29/227 (12.8%)                           | 1.42 (0.78–2.60) | .254  |                      |        |
| HIV positive                             | 8/78 (10.3%)                             | 1.11 (0.47–2.63) | .815  |                      |        |
| Rimming in the Last 12 Months            |                                          |             |        |                      |        |
| No                                       | 6/142 (4.2%)                             | 1 (ref)     | 1 (ref)|                      |        |
| Yes                                      | 51/363 (14.0%)                           | 3.71 (1.55–8.84) | .003  | 3.32 (1.38–7.97)     | .007  |
| Can’t remember                           | 0/14 (0%)                                | -           | -      |                      | -      |
| Group Sex in the Last Month              |                                          |             |        |                      |        |
| No                                       | 35/396 (8.8%)                            | 1 (ref)     |        |                      |        |
| Yes                                      | 22/123 (17.9%)                           | 2.25 (1.26–4.00) | .006  | 2.00 (1.11–3.60)     | .021  |
| Used Party Drugs in the Last Month       |                                          |             |        |                      |        |
| No                                       | 47/451 (10.4%)                           | 1 (ref)     |        |                      |        |
| Yes                                      | 10/68 (14.7%)                            | 1.48 (0.71–3.09) | .295  |                      |        |
| Sex Overseas in the Last 12 Months       |                                          |             |        |                      |        |
| No                                       | 15/165 (9.1%)                            | 1 (ref)     |        |                      |        |
| Yes                                      | 16/105 (15.2%)                           | 1.80 (0.85–3.81) | .126  |                      |        |
| Unknown/Declined/Missing                 | 26/249 (10.4%)                           | 1.17 (0.60–2.27) | .653  |                      |        |
| Pharyngeal Gonorrhea                     |                                          |             |        |                      |        |
| Negative                                 | 50/460 (10.9%)                           | 1 (ref)     |        |                      |        |
| Positive                                 | 3/29 (11.1%)                             | 0.95 (0.28–3.24) | .930  |                      |        |
| Not tested                               | 4/30 (12.1%)                             | 1.26 (0.42–3.76) | .677  |                      |        |
| Urethral Gonorrhea                       |                                          |             |        |                      |        |
| Negative                                 | 51/486 (10.5%)                           | 1 (ref)     |        |                      |        |
| Positive                                 | 1/6 (16.7%)                              | 1.71 (0.20–14.89) | .629  |                      |        |
| Not tested                               | 5/27 (18.5%)                             | 1.94 (0.70–5.34) | .200  |                      |        |
| Anorectal Gonorrhea                      |                                          |             |        |                      |        |
| Negative                                 | 51/468 (10.9%)                           | 1 (ref)     |        |                      |        |
| Positive                                 | 2/18 (11.1%)                             | 1.02 (0.23–4.57) | .977  |                      |        |
| Not tested                               | 4/33 (12.1%)                             | 1.13 (0.38–3.34) | .828  |                      |        |
| Pharyngeal Chlamydia                     |                                          |             |        |                      |        |
| Negative                                 | 51/486 (10.5%)                           | 1 (ref)     |        |                      |        |
| Positive                                 | 2/7 (28.6%)                              | 3.41 (0.65–18.04) | .149  |                      |        |
| Not tested                               | 4/26 (15.4%)                             | 1.55 (0.51–4.68) | .436  |                      |        |
| Urethral Chlamydia                       |                                          |             |        |                      |        |
| Negative                                 | 52/475 (10.9%)                           | 1 (ref)     |        |                      |        |
| Positive                                 | 0/17 (0%)                                | -           | -      |                      | -      |
| Not tested                               | 5/27 (18.5%)                             | 1.85 (0.67–5.09) | .234  |                      |        |
| Anorectal Chlamydia                      |                                          |             |        |                      |        |
| Negative                                 | 44/442 (10.0%)                           | 1 (ref)     |        |                      |        |
| Positive                                 | 9/44 (20.5%)                             | 2.33 (1.05–5.16) | .038  |                      |        |
| Not tested                               | 4/33 (12.1%)                             | 1.25 (0.42–3.71) | .691  |                      |        |

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; PrEP, pre-exposure prophylaxis.
Acknowledgments

Regardless of these limitations, our findings have direct public health implications for the prevention of gastrointestinal infections particularly in relationship to the role of asymptomatic carriage. We found that 11% of MSM had a pathogen detected and that oroanal sex is common. In this context, it is likely that a substantial incidence of infection relates to asymptomatic transmission during oroanal sex. More important, a recent study asked MSM attending an STI clinic what sexual practices they would be likely to forego to prevent an STI, and approximately 50% said they would be willing to stop rimming [16]. Men who have sex with men should be advised in health promotional messages that the practice of rimming increases the risk for carriage of asymptomatic enteric pathogens.

CONCLUSIONS

Regardless of these limitations, our findings have direct public health implications for the prevention of gastrointestinal infections particularly in relationship to the role of asymptomatic carriage. We found that 11% of MSM had a pathogen detected and that oroanal sex is common. In this context, it is likely that a substantial incidence of infection relates to asymptomatic transmission during oroanal sex. More important, a recent study asked MSM attending an STI clinic what sexual practices they would be likely to forego to prevent an STI, and approximately 50% said they would be willing to stop rimming [16]. Men who have sex with men should be advised in health promotional messages that the practice of rimming increases the risk for carriage of asymptomatic enteric pathogens.

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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.

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