High Prevalence of Rectal *Chlamydia trachomatis* Infection With the Same Genotype as Urogenital Infection in Female Outpatients in Sexually Transmitted Disease Clinics in China

Yan Han, Kai Chen, Jing-Wei Liu, Bang-Yong Zhu, Ke Zhou, Mei-Qin Shi, Wen-Qi Xu, Tulip A. Jhaveri, Yue-Ping Yin, and Xiang-Sheng Chen

*Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, Nanjing, Jiangsu, China; National Center for STD Control, Chinese Center for Disease Control and Prevention, Nanjing, Jiangsu, China; Institute of Dermatology, Guangxi Autonomous Region, Nanning, Guangxi, China; Tianjin Academy of traditional Chinese Medicine Affiliated Hospital, Tianjin, China; Division of Medical Microbiology, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts, USA; and Division of Infectious Diseases, University of Mississippi Medical Center, Jackson, Mississippi, USA

**Background.** Little is known about rectal *Chlamydia trachomatis* (CT) infection in outpatients attending sexually transmitted disease (STD) clinics in China. In this study, we aimed to explore the clinical and epidemiologic features of rectal CT infection in this population.

**Methods.** A cross-sectional study was conducted among patients attending STD clinics in Tianjin and Guangxi provinces of China from June 2018 to August 2020. Bivariate and multivariate logistic regression analysis were developed to explore the association of different risk factors for urogenital and rectal CT infection.

**Results.** The prevalence of urogenital and rectal CT was 11.2% (154/1374) and 4.9% (68/1377), respectively. The rectal CT prevalence among female and male patients was 7.8% (60/767) and 1.3% (8/610), respectively. The most common genotype in urogenital CT–positive samples was genotype E (29.9%), while the most common genotype among rectal CT–positive samples was genotype J (23.4%). More than 85% (52/60) of women infected with rectal CT were co-infected with urogenital CT. About 90.0% (36/40) of women shared similar genotypes between rectal and urogenital samples. Females and patients infected with urogenital CT were deemed to be at an increased risk for rectal CT infection. A high proportion of rectal CT infection had concurrent urogenital CT infection, especially in women, and most of the co-infections were shared among the same genotypes.

**Conclusions.** It would be prudent to encourage awareness and introduce detection tests and treatment strategies for rectal CT infection particularly in female patients visiting STD clinics in China.

**Keywords.** *Chlamydia trachomatis*; genotype; rectal infection; sexually transmitted disease clinics.

*Chlamydia trachomatis* (CT) is the most common sexually transmitted pathogen across the world and is one of the major contributors of overall prevalence of sexually transmitted infections (STIs) globally. Based on the 2018 global STI surveillance from the World Health Organization (WHO), global estimation of new CT cases in 2016 was 127.2 million [1]. Most individuals infected with chlamydia are asymptomatic. If left untreated, chlamydia initiates an inflammatory and immunological process leading to complications such as urethritis in men or cervicitis, pelvic inflammatory syndromes [2], and infertility [3] in women. It has also been shown to increase the risk of HIV transmission [4]. The mean duration of CT infection is 1.36 years [5]; the higher the prevalence of untreated infection, the more slowly clearance occurs, facilitating easier spread between partners and higher community transmission [6].

Various epidemiologic studies have shown that the rate of rectal chlamydia infection is very high not only in men who have sex with men (MSM) [7] but also in women and men who have sex with women [8]. In a Chinese study conducted on rectal CT prevalence among the general population, the pooled prevalence of urogenital CT among the general population was 2.9% (95% CI, 2.4%–3.5%) [9] and the rectal prevalence of CT in MSM was 15.6% [10]. Rectal *Chlamydial* infections can cause rectal pain, bleeding, and discharge, as well as proctitis [11]. They may also increase the risk of HIV acquisition [12] but are most often asymptomatic [13]. As a result, many rectal chlamydia infections are undiagnosed and untreated, and they eventually become a potential reservoir for ongoing transmission [14]. Rectal testing for CT is an emerging area that
should be considered in both men and women. The US Food and Drug Administration cleared commercially diagnostic tests for extragenital testing for CT in 2019 [15], but there are still no available diagnostic tests for rectal testing for CT in China. Rectal CT testing has not always been a part of routine sexually transmitted disease (STD) screening, particularly in asymptomatic patients attending STD clinics in China.

In this study, we (1) evaluate the prevalence of rectal CT infections in patients attending STD clinics, (2) identify potential risk factors for rectal CT infection, and (3) analyze the genotypic relationship between urogenital and rectal CT infection. The findings of this study are intended to help us understand the clinical and epidemiologic features of rectal CT and revise the guidelines for diagnosis and management of extragenital CT in China.

METHODS

Study Participants
A cross-sectional study was conducted between June 2018 and August 2020. Participants included individuals attending 2 outpatient STD clinics in China: (1) Tianjin Academy of Traditional Chinese Medicine Affiliated Hospital, located in Northern China and (2) Guangxi Institute of Dermatology, located in Southern China. This study was conducted in accordance with the Declaration of Helsinki and was reviewed and approved by the Institutional Review Board of the Institute of Dermatology, the Chinese Academy of Medical Sciences, and Peking Union Medical College (approval number 2017-LS-021). Participants were consecutively approached for eligibility and included in the study if they met the following criteria: (1) age >18 years, (2) willing to provide urine, vaginal, and rectal swabs, (3) and willing to fill out an anonymous questionnaire that consisted of questions regarding sociodemographic characteristics, sexual behavior, and STD history. More than 95% patients consented to participate in this study. All participants signed informed consent.

Specimen Collection
Male participants provided urine specimens and rectal swabs, while female participants provided vaginal and rectal swabs. Male participants self-collected 10–15 mL of first void urine (FVU) in urine cup. Approximately 5–7 mL of urine was transferred into the Cobas PCR Media tube with preservation solution to make sure the urine mixture was in the middle of the highest and lowest scale lines using disposable pipettes (Roche Molecular Systems, South Branchburg, NJ, USA) by local technicians. The technicians collected the vaginal and rectal swabs and directly transferred them into the Cobas PCR Media tubes, which were stored at 4°C in refrigerators in local hospitals. These samples were transported in batches at 18°C–25°C to the STD reference laboratory at the National Center for STD Control.

Laboratory Testing
Cobas 4800 CT/NG assay (Roche Molecular Systems, NJ, USA) was used per the manufacturer’s instructions with minor modifications to detect urogenital and rectal CT and Neisseria gonorrhoeae (NG) in the STD reference laboratory. Vaginal and rectal swabs were removed before testing. The Cobas x480 instrument was used to extract nucleic acid from urogenital and rectal samples and distribute polymerase chain reaction (PCR) reaction mixture. The Cobas x480 analyzer was used to perform PCR amplification and detection in a fully automated fashion.

From urogenital and rectal CT–positive samples, genomic DNA was extracted, which remained preserved in Cobas PCR Media using Tianlong nucleic acid extraction reagent (Xi’an Tianlong Science & Technology Co., LTD, Shaanxi, China) in a Tianlong GeneRotex 96 nucleic acid extractor according to the manufacturer’s instructions. The template DNA amplified the ompA gene, followed by the nested PCR method as described in the MLST database website (http://mlstdb.bmc.uu.se) of Uppsala University with minor modifications. There were 2 pairs of primers (inner and outer) for amplification of the ompA gene and 2 primers for sequencing. The detailed information for the primers is shown in Table 1. All the primers were synthesized by Invitrogen Corporation (Invitrogen Corporation, Carlsbad, CA, USA). In the first run for nested PCR, the total PCR reaction mixture was 25 μL:1 μL each for outer primers 118F and 1163R, 12.5 μL for 2×Vazyme Taq-Master Mix, 5 μL for the DNA template of CT-positive samples, and 5.5 μL for ultrapure water. CT serovar E-bour strain (American Type Culture Collection Corporation, Manassas, VA, USA) was used as the positive control, and water was used as the negative control. Each batch of testing included a positive and negative control and was performed under the following conditions on Thermo cycle 2720 (Applied Biosystems, USA): initial denaturation at 95°C for 15 minutes, denaturation at 94°C for 45 seconds, annealing at 60°C for 45 seconds, elongation at 72°C for 90 seconds for 40 cycles, 72°C final elongation for 10 minutes, and preservation at 4°C. The PCR reaction mixture for the second run included inner primers MOMP87 and RVS1059, 2×Vazyme Taq-Master Mix, and water, and the products from the first run were used as the templates. The amplification procedure in the

| Table 1. Primer Pairs Used for PCR Amplification and Sequencing of ompA Fragment |
|-----------------------------|-----------------------------|-----------------------------|
| Name | Function | Sequence |
| 118F | Outer primer | 5′-ATTGCTACAGGACATCTTGTGC-3′ |
| 1163R | Outer primer | 5′-CGAATTGTGACATTACAGTGAG-3′ |
| MOMP87 | Inner primer | 5′-TGAAACCAAAGCTTATGATGACGAGA-3′ |
| RVS1059 | Inner primer | 5′-GCAATACCGGGAGATTTCTGATCTTGTGAG-3′ |
| ctr200F | Sequencing | 5′-TTAGGGCTCTCCCTTCTTTCCTTCCATYAGCTCAATC-3′ |
| ctr254R | Sequencing | 5′-GCATCGTCTATGCTTACATAGAGGCATC-3′ |

Abbreviation: PCR, polymerase chain reaction.
second run was same as that used in the first run. Purified PCR products from the second run were bidirectionally sequenced using the sequencing primers. The quality of the raw sequence data was checked using FinchTV, version 1.5.0, and then the bidirectional sequences for every sample were assembled using DNAstar, version 7.1. The resulting assembled sequence was used for genotyping based on the BLAST similarity search tool on the National Center for Biotechnology Information website (www.ncbi.nlm.nih.gov).

Data Analysis

Collected questionnaires and experimental data were entered into an Excel format database by a technician. Another technician verified the database according to the original questionnaires and experimental data. IBM SPSS Statistics for Windows, version 22.0 (IBM Corp, New York, NY, USA), was used for statistical data analyses. Binary logistic regression was conducted to explore the associations of different risk factors for CT infection, with odds ratios and corresponding 95% CIs concurrently estimated. Variables associated with urogenital or rectal CT at \( P \leq .10 \) in bivariate logistic regressions were included in multivariate logistic regression models to identify independent risk factors. Adjusted odds ratios (AORs) and their 95% CIs were estimated in a multivariate logistic regressions model. Variables associated with urogenital or rectal CT at \( P < .05 \) in multivariate logistic regressions were considered statistically significant.

RESULTS

During the study period, 1563 participants were enrolled in the study, of whom 1382 were included in the final analysis. Of the 181 who were excluded, 15 were aged <18 years, 19 refused to collect rectal swabs, and 147 rectal samples were collected incorrectly by nurses. The mean age of participants was 37.9 years (ranging from 18 to 72 years). Five hundred fifty-three participants (40.0%) were enrolled at Tianjin Academy of Traditional Chinese Medicine Affiliated Hospital, 614 were male (44.4%), and 318 (23.0%) were unmarried. Nearly all participants reported their sexual orientation, 2 reported homosexual orientation, and 3 reported bisexual orientation. Four male patients (0.7%, 4/611) and 3 female patients (0.4%, 3/761) reported having had anal intercourse in the past 2 weeks. Two-thirds of the included participants (67.0%, 926/1382) presented with urogenital symptoms, while none presented with rectal symptoms (Table 2).

| Item                        | No. of Participants Responding | Proportion, % |
|-----------------------------|--------------------------------|----------------|
| Province                    |                                |                |
| Tianjin                     | 553                            | 40.0           |
| Guangxi                     | 829                            | 60.0           |
| Gender                      |                                |                |
| Male                        | 614                            | 44.4           |
| Female                      | 768                            | 55.6           |
| Ethnicity                   |                                |                |
| Han                          | 1036                           | 75.1           |
| Minority nationality        | 343                            | 24.9           |
| Education                   |                                |                |
| Primary school              | 50                             | 7.1            |
| Middle school               | 184                            | 26.1           |
| High school                 | 156                            | 22.1           |
| Undergraduate               | 299                            | 42.4           |
| Graduate                    | 17                             | 2.4            |
| Marriage                    |                                |                |
| Unmarried                   | 318                            | 23.0           |
| Married                     | 1002                           | 72.5           |
| Divorced                    | 56                             | 4.1            |
| Widowed                     | 4                              | 0.3            |
| Other                       | 2                              | 0.1            |
| Sexual orientation          |                                |                |
| Heterosexual                | 1374                           | 99.4           |
| Homosexual                  | 2                              | 0.1            |
| Bisexual                    | 3                              | 0.2            |
| Medical insurance           |                                |                |
| Medical insurance system for urban employee | 411 | 29.8 |
| New rural cooperative medical system | 538 | 39.0 |
| Commercial insurance        | 20                             | 1.5            |
| None                        | 409                            | 29.7           |
| Income                      |                                |                |
| <30,000 RMB                 | 246                            | 18.0           |
| 30,000-50,000 RMB           | 373                            | 27.2           |
| 50,000-80,000 RMB           | 511                            | 37.3           |
| 80,000-100,000 RMB          | 171                            | 12.5           |
| >100,000 RMB                | 68                             | 5.0            |
Of the 1382 patients, 1380 participants provided urogenital samples, consisting of 612 urine samples and 768 vaginal swabs. All participants provided rectal samples. Six urogenital samples and 5 rectal swabs were not amplified effectively with the Roche PCR test. The urogenital prevalence for CT and NG was 11.2% (154/1374; 95% CI, 9.6%–13.0%) and 5.7% (78/1374; 95% CI, 4.5%–7.1%), respectively. The rectal prevalence for CT and NG was 4.9% (68/1377; 95% CI, 3.9%–6.2%) and 2.5% (35/1377; 95% CI, 1.8%–3.6%), respectively. The rectal CT prevalence was 7.8% (60/767; 95% CI, 6.1%–10.0%) and 1.3% (8/610; 95% CI, 0.6%–2.7%) in female and male patients, respectively. Fifty-five patients were coinfected with rectal and urogenital CT (prevalence, 4.0%; 55/1374; 95% CI, 3.1%–5.2%), while 25 were coinfected with rectal and urogenital NG (prevalence, 1.8%; 25/1374; 95% CI, 1.2%–2.7%).

Of the 222 CT-positive samples, 184 (82.9%) isolates were successfully sequenced and analyzed; 137 isolates were from urogenital sources, while 47 were from rectal sources. Ten genotypes were found in urogenital samples, and 8 were found in rectal samples. No genotype was found in mixed infection from either urogenital or rectal samples. The most common genotypes in urogenital CT-positive samples were genotypes...
E (41/137, 29.9%), J (27/137, 19.7%), and D (21/137, 15.3%). The most common genotypes in rectal samples were genotypes J (11/47, 23.4%), E (10/47, 21.3%), and D (9/47, 19.2%) (Figure 1). There was no statistically significant difference in distribution of CT genotypes between the urogenital and rectal samples ($\chi^2 = 3.558, P = .936$). Thirty-eight of 42 rectal samples (90.5%) had the same genotype as that of urogenital samples. Of these 38, 2 samples were from men and 36 were from women. Genotype L, which causes lymphogranuloma venereum, was not found in this study.

Bivariate logistic regression analyses showed that urogenital CT was significantly associated with different zones, gender, age, marital status, medical insurance status, number of sexual partners, genital symptoms, and infection with urogenital NG. These 8 variables were selected in the final multivariate analysis for urogenital CT infection. After adjusting for potential confounders, the following variables were found to be significantly associated with urogenital CT: being from Tianjin (AOR, 0.981; 95% CI, 0.969–0.993), age <25 years (AOR, 2.145; 95% CI, 1.287–3.572), and urogenital NG infection (AOR, 3.43; 95% CI, 1.99–5.912) (Table 3). Seven variables—gender, age, marital status, medical insurance status, STD history, infection with rectal NG, and urogenital CT—were used in the multivariate analysis for rectal CT infection. Variables found to be significantly associated with rectal CT were female gender (AOR, 16.727; 95% CI, 6.986–40.050) and urogenital CT infection (AOR, 95.391; 95% CI, 45.29–200.914) (Table 4).

**DISCUSSION**

To our knowledge, this is the first analysis of rectal *Chlamydia* infection and genotypes among STD clinic attendees in China. The findings from this study indicate that among male STD clinic attendees, the prevalence of rectal CT infection (1.3%) was lower than urogenital CT infection (13.7%) and lower compared with previous prevalence studies among MSM patients in China (15.5%) [10, 16]. Among female participants, the prevalence rates of rectal CT infection and urogenital CT infection were similar (7.8% and 9.3%, respectively), and comparable to the median prevalence in female patients in many developed countries [8, 17]. The total prevalence of rectal CT infection (2.5%) in this study was significantly lower than the urethral

**Table 3. Risk Factors Associated With Increased Risk of Genital CT Among STI Clinic Attendees in China**

| Risk Factors | Levels | Prevalence, % (no./No.) | OR (95% CI) | AOR (95% CI) |
|-------------|--------|--------------------------|-------------|-------------|
| Province    | Tianjin | 7.6 (42/552)             | 0.980 (0.969–0.992)* | 0.981 (0.969–0.993)# |
|             | Guangxi | 13.6 (112/822)            | Reference    | Reference    |
| Gender      | Male    | 13.7 (83/607)            | 1.553 (1.109–2.174)* | 1.195 (0.818–1.747) |
|             | Female  | 9.3 (71/767)             | Reference    | Reference    |
| Age         | ≤25 y   | 20.8 (38/183)            | 2.429 (1.619–3.642)* | 2.145 (1.287–3.572)# |
|             | >25 y   | 9.7 (116/1374)           | Reference    | Reference    |
| Education   | Basic   | 11.2 (26/233)            | 0.724 (0.448–1.172) | Reference    |
|             | High    | 14.8 (69/467)            | Reference    | Reference    |
| Marriage    | Married | 15.2 (57/36)             | 1.600 (1.168–2.358)* | 1.163 (0.756–1.788) |
|             | Single  | 9.7 (97/988)             | Reference    | Reference    |
| Ethnicity   | Han     | 10.7 (111/1033)          | 0.848 (0.581–1.239) | Reference    |
|             | Minority nationality | 12.4 (42/338) | Reference    | Reference    |
| Sexual orientation | Homosexual/bisexual | 0 (0/5) | – | Reference |
| | Heterosexual | 11.2 (153/1386) | Reference | Reference |
| Insurance   | No      | 15.3 (62/406)            | 1.708 (1.209–2.413)* | 1.266 (0.87–1.842) |
|             | Yes     | 9.5 (92/964)             | Reference    | Reference    |
| Income/y, renminbi yuan | <80 000 | 11.1 (125/1124)          | 0.934 (0.604–1.444) | Reference    |
|             | ≥80 000 | 11.8 (28/237)            | Reference    | Reference    |
| STD history | Yes     | 9.7 (23/238)             | 0.819 (0.513–1.307) | Reference    |
|             | No      | 11.6 (131/1134)          | Reference    | Reference    |
| No. of sexual partners | >1 | 14.5 (47/325)          | 1.457 (1.006–2.108)* | 1.387 (0.916–2.102) |
|             | 1      | 10.4 (104/1000)          | Reference    | Reference    |
| Symptoms    | Yes     | 12.4 (114/918)           | 1.475 (1.009–2.154)* | 1.317 (0.887–1.956) |
|             | No      | 8.8 (40/456)             | Reference    | Reference    |
| Anal intercourse | Yes | 0.0 (0/7) | – | Reference |
|             | No     | 11.3 (146/1295)          | Reference    | Reference    |
| Urogenital infection | NG | 34.6 (27/78)          | 4.873 (2.952–8.043)* | 3.431 (0.99–5.912)# |
|             | Non-NG | 9.8 (127/1296)          | Reference    | Reference    |

Abbreviations: AOR, adjusted odds ratio; CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*; OR, odds ratio; STD, sexually transmitted disease; STI, sexually transmitted infection.

*P < .1.

#P < .05.
CT prevalence in this study (11.2%) and rectal CT prevalence in MSM in previous studies in China [10, 16]. This suggests that the high-risk behaviors related to rectal CT transmission in STD clinic attendees are different from urogenital transmission and different from rectal CT transmission in MSM. A total of 222 cases with CT infection were identified—55 of whom (24.8%) had infection at both anatomic sites. Thirteen of 68 rectal CT infections (19.1%) would be missed in absence of rectal testing in this study; this phenomenon was consistent with other studies that have been published thus far [18, 19].

High rates of concurrent genital and rectal chlamydial infections in female patients should call our attention. Doxycycline and azithromycin are first-line antibiotics for the treatment of CT infection. However, our findings suggest that the effectiveness of doxycycline and the effectiveness of azithromycin for the treatment of rectal and urogenital chlamydia are different. Azithromycin had lower efficacy compared with doxycycline for the treatment of rectal chlamydia infection [20, 21]. This suggests that doxycycline would be a reasonable choice to treat female urogenital CT infection in order to treat a presumed undiagnosed rectal CT infection in the absence of rectal testing.

The genotype distribution in rectal CT infection had no significant difference compared with urogenital CT infection ($\chi^2 = 3.558; P = .936$); the prevalent genotypes in rectal CT infection were genotypes J (23.4%), E (21.3%), and D (19.2%), which were also very common in urogenital CT infection [E (29.9%), J (19.7%), and D (15.3%)] in all outpatients in STD clinics; 90.5% (38/42) of rectal infections had the same genotype as urogenital infections. These findings suggest a strong correlation between rectal CT infection and urogenital infection. The most common genotypes associated with rectal CT infection in this population were different from Chinese MSM groups reported in previous studies [16, 22, 23], where the most prevalent genotypes were genotypes D and G, which accounted for >70% of rectal CT infections. This difference may partly be explained by differences.
in sexual practices among outpatients in STD clinics and MSM, with insufficient overlap between these 2 groups in China.

We found that risk factors for CT infections from urogenital and anorectal sites were different. In our study, age <25 and urogenital NG infection were independent risk factors for urogenital CT infection, while female gender and urogenital CT infection were independent risk factors for rectal CT infection. Age <25 is a known risk factor in chlamydial management; women age <25 are encouraged to test for CT every year in certain developed countries [24, 25]. CT/NG co-infection is very common [26], with an antichlamydial regimen for treatment of uncomplicated NG suggested in most STI guidelines [25, 27]. Although no consensus has been reached among experts regarding the dual antimicrobial therapy of choice for uncomplicated NG, mandatory combination with an antichlamydial agent may reduce the spread of chlamydia.

In line with our results, previous studies have suggested that rectal CT could be caused by spread of cervical infection via the perianal region to the rectum [28]. In our study, 86.7% (52 in 60) of the female rectal CT–infected patients had a concurrent urogenital infection, and 87.5% (35/40) of them had the same genotypes. Self-spread of urogenital infection to the rectum by auto-inoculation or contamination from post-toilet wiping behavior could be possible [29, 30].

Our study had the following limitations. First, none of the patients reported proctitis. A possible explanation could be lack of rectal symptoms in most patients infected with rectal CT [31]. Another possibility is that most patients who develop proctitis would choose the proctology department rather than an STD clinic for treatment; these patients could not be recruited in this study. Second, high-risk behaviors such as anal intercourse and number of sexual partners were found to have no significant correlation with CT infection. It is possible that this sensitive information would be deliberately concealed by the patients, leading to underestimation of high-risk sexual behavior. Third, pharyngeal swabs were not collected in this study; hence we cannot explain whether infection at the anorectal site in absence of urogenital CT infection or with a genotype different from urogenital infection was from the gastrointestinal tract through oral sex [32]. Lastly, the cross-sectional nature of this study would be less effective in studying the natural history and transmission capacity of rectal CT infection compared with a prospective study. How some patients develop rectal CT infection without anal intercourse or urogenital infection cannot be explained.

CONCLUSIONS

A high proportion of patients with rectal CT infection had concurrent urogenital CT infection, especially women, and most of these coinfections shared the same genotypes. Screening for rectal CT infection might be more important for female patients visiting STD clinics regardless of rectal symptoms and irrespective of anal intercourse. Test reagents and treatment strategies for rectal CT infection should be introduced in China as soon as possible.

Acknowledgments

We are grateful to the collaborating STD clinics where this study took place and to the participants of this study for their cooperation. Author contributions. Y.H. and Y.-P.Y. conceived of the study and supervised all aspects of its implementation. Y.H., K.C., and J.-W.L. contributed to conceptualizing ideas and designing the study. Y.H., K.C., J.-W.L., B.-Y.Z., K.Z., M.-Q.S., and W.-Q.X.X. participated in recruiting the subjects and conducted the experiment. Y.H., J.-W.L., B.-Y.Z., and K.Z. provided input regarding analysis of the data. Y.H., Y.-P.Y., T.-A.J., and X.-S.C. interpreted findings and reviewed drafts of the manuscript. All authors read and approved the final manuscript.

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, Nanjing, China, or the National Center for STD Control, Chinese Center for Disease Control and Prevention, Nanjing, China.

Financial support. This work was supported by the Chinese Academy of Medical Sciences Initiative for Innovative Medicine (grant 2016-12M-3-021). Potential conflicts of interest. All 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. World Health Organization. Report on global sexually transmitted infection surveillance. 2018. Available at: https://apps.who.int/iris/bitstream/handle/10665/277258/9789241565691-eng.pdf?sequence=5&isAllowed=y. Accessed 11 August 2021.
2. Baud D, Regan L, Greub G. Emerging role of Chlamydia and Chlamydia-like organisms in adverse pregnancy outcomes. Curr Opin Infect Dis 2008; 21:70–6.
3. Ginocchio CC, Chapin K, Smith JS, et al. Prevalence of Trichomonas vaginalis and coinfection with Chlamydia trachomatis and Neisseria gonorrhoeae in the United States as determined by the Aptima Trichomonas vaginalis nucleic acid amplification assay. J Clin Microbiol 2012; 50:2601–8.
4. Cohen CR, Plummer FA, Mugo N, et al. Increased interleukin-10 in the endocervical secretions of women with non-ulcerative sexually transmitted diseases: a mechanism for enhanced HIV-1 transmission? AIDS 1999; 13:327–32.
5. Price MJ, Ades AE, Angelis DD, et al. Mixture-of-exponential models to explain heterogeneity in studies of the duration of Chlamydia trachomatis infection. Stat Med 2013; 32:1547–60.
6. Lewis J, Price MJ, Horner PJ, White PJ. Genital Chlamydia trachomatis infections clear more slowly in men than women, but are less likely to become established. J Infect Dis 2017; 216:237–44.
7. Smolak A, Chemaiteilly H, Herveg JG, et al. Epidemiology of Chlamydia trachomatis in the Middle East and North Africa: a systematic review, meta-analysis, and meta-regression. Lancet Glob Health 2019; 7:e1197–225.
8. Chan PA, Robinson A, Montgomery M, et al. Extrapulmonary infections caused by Chlamydia trachomatis and Neisseria gonorrhoeae: a review of the literature. Infect Dis Obstet Gynecol 2016; 2016:5758387.
9. Huai P, Li F, Chu T, et al. Prevalence of genital Chlamydia trachomatis infection in the general population: a meta-analysis. BMC Infect Dis 2020; 20:589.
10. Zhou Y, Cai YM, Li SL, et al. Anatomical site prevalence and genotypes of Chlamydia trachomatis infections among men who have sex with men: a multisite study in China. BMC Infect Dis 2019; 19:1041.
11. de Vries HJ, Zingoni A, White JA, et al. 2013 European guideline on the management of proctitis, proctocolitis and enteritis caused by sexually transmitted pathogens. Int J STD AIDS 2014; 25:465–74.
12. Bernstein KT, Marcus JL, Nieri G, et al. Rectal gonorrhoea and chlamydia reinfection is associated with increased risk of HIV seroconversion. J Acquir Immune Defic Syndr 2010; 53:537–43.
13. Otsemo F, Ngéty G, Okall D, et al. Incident gonorrhea and chlamydia among a prospective cohort of men who have sex with men in Kisumu, Kenya. Sex Transm Infect 2020; 96:521–7.
14. Hemsley S, Canfield PJ. Proctitis associated with chlamydial infection in a koala. Aust Vet J 1996; 74:148–50.
15. Adamson PC, Pandori MW, Doernberg SB, et al; Antibacterial Resistance Leadership Group. Analytical evaluation of the abbott RealTime CT/NG assay for detection of Chlamydia trachomatis and Neisseria gonorrhoeae in rectal and pharyngeal swabs. J Mol Diagn 2020; 22:811–6.

16. Zhang X, Jia M, Chen M, et al. Prevalence and the associated risk factors of HIV, STIs and HBV among men who have sex with men in Kunming, China. Int J STD AIDS 2017; 28:1115–23.

17. Dewart CM, Bernstein KT, DeGroote NP, et al. Prevalence of rectal chlamydial and gonococcal infections: a systematic review. Sex Transm Dis 2018; 45:287–93.

18. Jann JT, Cunningham NJ, Assaf RD, Bolan RK. Evidence supporting the standardisation of extragenital gonorrhoea and chlamydia screenings for women. Sex Transm Infect. 2021;sextrans-2020-054533.

19. Janssen KJH, Wolffs PFG, Hoebe CJPA, et al. Determinants associated with viable genital or rectal Chlamydia trachomatis bacterial load (FemCure). Sex Transm Infect. In press.

20. Kong FY, Tubrizi SN, Fairley CK, et al. The efficacy of azithromycin and doxycycline for the treatment of rectal chlamydia infection: a systematic review and meta-analysis. J Antimicrob Chemother 2015; 70:1290–7.

21. Dukers-Muijrers NHTM, Wolffs PFG, De Vries H, et al. Treatment effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal Chlamydia trachomatis infections in women: a multicenter observational study (FemCure). Clin Infect Dis 2019; 69:1946–54.

22. Li JH, Cai YM, Yin YP, et al. Prevalence of anorectal Chlamydia trachomatis infection and its genotype distribution among men who have sex with men in Shenzhen, China. Jpn J Infect Dis 2011; 64:143–6.

23. Qin X, Zheng H, Xue Y, et al. Prevalence of Chlamydia trachomatis genotypes in men who have sex with men and men who have sex with women using multilocus VNTR analysis-ompA typing in Guangzhou, China. PLoS One 2016; 11:e0159658.

24. Unemo M, Seifert HS, Hook EW 3rd, et al. Gonorrhoea. Nat Rev Dis Primers 2019; 5:79.

25. Bignell C, Unemo M; European STI Guidelines Editorial Board. 2012 European guideline on the diagnosis and treatment of gonorrhoea in adults. Int J STD AIDS 2013; 24:85–92.

26. Leonard CA, Schoborg RV, Low N, et al. Pathogenic interplay between Chlamydia trachomatis and Neisseria gonorrhoeae that influences management and control efforts—more questions than answers? Curr Microbiol Rep 2019; 6:182–91.

27. National Center for STD Control, Chinese Center for Disease Control and Prevention; Venereology Group, Chinese Society of Dermatology; Subcommittee on Venereology, China Dermatologist Association. Guidelines for diagnosis and treatment of syphilis, gonorrhea and genital Chlamydia trachomatis infection. Chin J Dermatol 2020; 53:168–79.

28. Sethupathi M, Blackwell A, Davies H. Rectal Chlamydia trachomatis infection in women. Is it overlooked? Int J STD AIDS 2010; 21:93–5.

29. Heijne JCM, van Lier GAFS, Hoebe CJPA, et al. What explains anorectal chlamydia infection in women? Implications of a mathematical model for test and treatment strategies. Sex Transm Infect 2017; 93:270–5.

30. Simpson S Jr, Blomfield P, Cornall A, et al. Front-to-back & dabbing wiping behaviour post-toilet associated with anal neoplasia & HR-HPV carriage in women with previous HPV-mediated gynaecological neoplasia. Cancer Epidemiol 2016; 42:124–32.

31. Ding A, Challenor R. Rectal Chlamydia in heterosexual women: more questions than answers. Int J STD AIDS 2014; 25:587–92.

32. Rank RG, Yeruva L. Hidden in plain sight: chlamydial gastrointestinal infection and its relevance to persistence in human genital infection. Infect Immun 2014; 82:1362–71.