

Prevalence of and risk factors for sexually transmitted infection with *Chlamydia trachomatis* to guide control measures: findings from the Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 2016–2017

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Abstract

Introduction: To inform *Chlamydia trachomatis* (CT) infection control, the objectives of the second Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 2016–2017 were to estimate the prevalence of and identify risk factors for CT infection among sexually experienced 18- to 49-year-olds in Slovenia.

Methods: Data were collected from a probability sample of the general population 18 to 49 years old. Respondents were invited to provide a urine specimen for CT testing. Data were analyzed using STATA 15 survey commands to account for stratification and clustering.

Results: Of 1,046 CT test results of sexually experienced respondents included in the analyses, the weighted prevalence of CT infection was 0.5% (95% confidence interval [CI]: 0.1–1.9) in men and 1.7% (95% CI: 0.9–3.3) in women. The highest prevalence was among women 18 to 24 years old (5.6%; 95% CI: 2.0–14.4). Women 18 to 49 years old with a new sex partner in the last year had higher odds of CT infection (adjusted odds ratio: 8.9, 95% CI: 2.5–31.9).

Conclusions: The introduction of annual opportunistic testing for CT should be considered for sexually active women < 25 years old, and testing should be offered at primary healthcare gynecology clinics to older women reporting a new sex partner during the past year.

Keywords: *Chlamydia trachomatis*, survey, general population, prevalence, sexual behavior, risk factors, Slovenia

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Introduction

Sexually transmitted infection (STI) with *Chlamydia trachomatis* (CT) is one of the most common curable STIs globally, with the highest prevalence in upper-middle income countries (1). CT infection is of public health concern because it can progress to damage the upper reproductive tract and cause complications, including pelvic inflammatory disease, tubal factor infertility, ectopic pregnancy, and chronic pelvic pain in women (2). In men, CT infection complications include epididymitis, orchitis, and chronic prostatitis, and it may also play a role in male infertility (3, 4). CT infection is straightforward to diagnose, and inexpensive and effective antibiotic treatments are available. However, the majority of CT infections are asymptomatic and often undiagnosed (2, 5). The World Health Organization (WHO) global health sector strategy on STIs 2016–2021, noted the importance of CT infection and stressed the need for further research to define strategies to control and measure these infections (6).

Based on the 2019 WHO estimate, in 2016 the prevalence of CT infection for the European region among individuals 15 to 49 years old was 2.2% (95% confidence interval [CI]: 1.5–3.0) in men and 3.2% (95% CI: 2.5–4.2) in women (1). These estimates were updated by a meta-analysis published in 2020 with similar CT prevalence estimates for men (2.5%; 95% CI: 1.7–3.4) and somewhat lower CT prevalence estimates for women (2.6%; 95% CI: 1.7–3.6), possibly due to a difference in the inclusion criteria for the studies (5). In both studies, CT point prevalence estimates were higher than the

corresponding 2012 WHO CT point prevalence estimates, but the uncertainty intervals of all these estimates overlapped (1, 5).

CT infection is the most commonly reported curable STI in Europe in general and in Slovenia, with the highest notification rates of newly diagnosed cases reported among young women (2, 7). Due to under-ascertainment and underreporting, the reported rates of newly diagnosed CT infections underestimate the true incidence (2, 7). In Slovenia, the overall annual reported rates of new diagnoses of CT infection between 2014 and 2018 varied between 11.9 and 16.0 cases per 100,000 and were the highest among young individuals (7). In 2018, the reported rate was 15.3 among men and 24.5 per 100,000 among women under 25 (7). Overall, the reported rates were approximately a tenth of the corresponding reported rates for European countries, which was mainly due to low Slovenian annual diagnostic testing rates, which varied between 175 and 220 CT tests per 100,000 between 2014 and 2018, but to a smaller extent also due to underreporting (7–9). In contrast, a rather high prevalence of CT infection among sexually experienced men and women 18 to 24 years old (4.7%; 95% CI: 2.2–8.5) was estimated in the first Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 1999–2000 (10). A review of studies in various Slovenian population groups also indicated a rather high prevalence of CT infection among 20- to 24-year-olds (11). This suggests that a large proportion of CT infections in Slovenia remain undiagnosed and untreated. The results of the European Centre for Disease Prevention and Control (ECDC) study of the burden of communicable diseases in Europe showed that in EU/EEA

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countries between 2009 and 2013 CT infection ranked 10th among 31 communicable diseases examined, with an estimated annual burden of 4.63 (95% CI: 2.16–9.03) disability-adjusted life years (DALYs) per 100,000 (12). To reduce transmission and adverse reproductive health outcomes in many countries, testing of asymptomatic individuals has been recommended for sexually active women and/or men younger than 25 or 30 and also for some older individuals with risk factors for STIs; for example, those that have had a new sex partner recently, more than one sex partner, concurrent partners, or a sex partner with an STI (13–17). As of 2021, such testing has not been recommended in Slovenia.

One of the objectives of the second Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 2016–2017 was to assess the prevalence of and identify risk factors for CT infection in the general population 18 to 49 years old to inform consideration of targeted opportunistic testing.

Methods

The methods used in the second Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health are described in detail in a study on the prevalence of STIs with CT, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, and *Trichomonas vaginalis* infection in Slovenia (18). In brief, a total of 4,000 individuals 18 to 49 years old were selected from the central population registry using a stratified two-stage probability sample of the general population. Data were collected between October 2016 and July 2017 at the respondents' homes using a combination of computer-assisted personal interviews and self-completion of questionnaires that included questions about sexual lifestyles. All respondents were invited to provide a urine sample for confidential testing for CT infection. Following signed informed consent, participants provided 4 to 5 ml of first-void urine using the FirstBurst device (19). The interviewers sent urine samples to the laboratory by mail within 24 hours. CT infection was detected with a specific in-house developed and validated real-time polymerase chain reaction (PCR) test. The primers used target two specific nucleotide sequences characteristic of CT: a 73 bp long section of the cryptic plasmid and an 89 bp long nucleotide sequence characteristic of the *ompA* gene located on the chromosome of CT. The *ompA* gene encodes the major outer membrane porin. Positive results were confirmed by Sanger sequencing of the amplicon. All individuals with CT infection were referred for treatment.

After testing for CT, first-void urine specimens of individuals that consented to delayed anonymous testing for other STIs were stored, as described in detail in the study on prevalence of STIs with CT, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, and *Trichomonas vaginalis* infection in Slovenia (18). We tested for other STIs with a commercially available multiplex real-time PCR (FTD Urethritis plus, Fast-Track Diagnostics), which also detects CT. The number of CT-positive results was equal to the number of positive results obtained with in-house real-time PCR testing of first-void urine specimens of all those individuals that consented to delayed anonymous testing for other STIs. The characteristics of positive individuals with any of the two tests were also perfectly matched for age and sex, underlining the validity of the in-house RT-PCR test for CT.

Statistical analyses were performed in Stata 15.1. Survey response and urine specimen collection rates were estimated from unweighted data. The sample of respondents that provided a urine specimen was weighted to match the distribution of sex, age, sta-

tistical region, and size and type of community of 18- to 49-year-olds from the Slovenian population in the Central Population Registry on January 1st, 2017. In all other analyses, survey (svy) commands were used to account for stratification, clustering, and weighting. Univariate and multivariate logistic regression were used to identify associations between having genital CT infection and selected risk factors in sexually experienced individuals 18 to 24 years old, women 18 to 49 years old, and women 25 to 49 years old. Sexual experience was defined as ever having heterosexual penetrative intercourse (vaginal, oral, and/or anal) and/or homosexual penetrative intercourse (oral and/or anal) or genital contact. Age group was treated as an a priori confounder. Other explanatory variables were selected according to risk factors identified in other studies and published guidelines for CT infection control (13–17, 20). Receiving payment for sex was included as a proxy for high-risk sexual behavior that may not be captured in other predictors (21). Variables were included in a series of logistic regression multivariate models if they were associated with the outcome at the significance level of $p < 0.1$ in univariate analyses. Only statistically significant ($p \leq 0.05$) sexual behavior variables plausibly associated with the outcome were included in the final multivariate models. Only records with complete data for all variables in the multivariate logistic regression models were used. Proportions of sexually experienced women that visited their general practitioner and/or gynecologist in the past year were estimated among all sexually experienced female respondents (regardless of whether they provided a urine sample).

Ethical approval for the second Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 2016–2017 was obtained from the Medical Ethics Committee of the Ministry of Health of the Republic of Slovenia (no. 38/08/16).

Results

Survey response, urine specimen collection, and testing rates in the second Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 2016–2017 are described in detail in the study on prevalence of STIs with CT, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, and *Trichomonas vaginalis* infection in Slovenia (18). Of 3,473 eligible individuals, 1,929 were interviewed and their data included in survey analyses, corresponding to a 55.5% survey response rate. A total of 1,100 urine specimens were collected, corresponding to a 57.0% urine specimen collection rate among the survey respondents. Only 1,046 CT test results of sexually experienced individuals were included in the analyses due to the following: four urine specimens arrived at the laboratory spilled, nine individuals were excluded from analyses because their corresponding interviews had major internal inconsistencies, and 41 tested individuals were not sexually experienced.

Out of 1,046 sexually experienced individuals with CT testing results included in the analysis, a total of 12 individuals, two men and 10 women (unweighted count), were found to be infected with CT. All were sexually experienced and none reported having had CT infection diagnosed previously. Both men belonged to the 18- to 24-year-old group. Among the 10 women, four belonged to the 18- to 24-year-old group, four to the 25- to 34-year-old group, and two to the 35- to 49-year-old group. All except one reported at least one visit to a general practitioner in the past year, and six also reported at least one visit to a gynecologist in the past year. Three out of four women from the 18- to 24-year-old group reported at least one visit to a gynecologist during the past year.

Among all sexually experienced women, 81.4% (95% CI: 78.7–83.8) of 18- to 49-year-olds had visited their general practitioner in the past year, and 73.9% (95% CI: 70.8–76.9) had visited their gynecologist in the past year. The respective shares among 18- to 24-year-old women were 84.4% (95% CI: 77.7–89.4) and 77.7% (95% CI: 68.9–84.5), and the respective shares among 25- to 49-year-old women were 80.9% (95% CI: 77.9–83.5) and 73.3% (95% CI: 69.9–76.5).

Table 1 shows the weighted prevalence estimates of CT infection for sexually experienced individuals, 18- to 49-year-olds, overall and by sex and age group. The prevalence was 0.5% (95% CI: 0.1–1.9) in men and 1.7% (95% CI: 0.9–3.3) in women. The prevalence was highest among women 18 to 24 years old (5.6%; 95% CI: 2.0–14.4) and decreased with increasingly older age groups in both sexes ($p < 0.05$).

Table 2 shows the association of CT infection with selected sexual behavior characteristics among sexually experienced individuals 18 to 24 years old. The prevalence of CT infection was 18 times higher among those that reported at least one new heterosexual partner in the past year in comparison to others ($p < 0.01$), 13 times higher among those that had accumulated at least three heterosexual partners in the past year in comparison to those with

none or only one ($p = 0.04$), nine times higher among those that reported not having used a condom consistently with at least two heterosexual partners during the preceding year in comparison to others ($p = 0.01$), six times higher among those that reported having accumulated at least 10 heterosexual partners during their life in comparison to others ($p = 0.03$), and five times higher among those that reported having ever had same-sex experience in comparison to those that did not ($p = 0.06$). Adjusting for possible confounding in multivariate analyses, the associations that remained statistically significant were reporting at least one new heterosexual partner in the past year (adjusted odds ratio [AOR]: 13.3; 95% CI: 1.0–171.5; $p = 0.05$), not having used a condom consistently with two heterosexual partners or more during the preceding year (AOR: 7.7; 95% CI: 1.3–45.5; $p = 0.03$), and having ever had same-sex experience (AOR: 13.5; 95% CI: 1.0–177.9; $p = 0.05$). Limiting the analysis to sexually experienced 18- to 24-year-old women reporting at least one new heterosexual partner in the past year remained statistically significant (AOR: 52.9; 95% CI: 5.1–554.6; $p < 0.01$) as well as having had their first heterosexual intercourse before age 16 (AOR: 20.3; 95% CI: 1.5–274.8; $p = 0.02$).

Table 3 shows the results of the univariate and multivariate analyses of association of CT infection with age and selected sexu-

Table 1 | Prevalence of sexually transmitted infections with *Chlamydia trachomatis* among sexually experienced individuals 18 to 49 years old, by sex and age group, Slovenia, 2016–2017.

Sex	18–24 years	25–34 years	35–49 years	All
Men				
% (95% CI)	3.4 (0.9–12.5)	0.0 (0.0–2.2) ^a	0.0 (0.0–1.2) ^a	0.5 (0.1–1.9)
UWT, WT denominator	67, 76	138, 166	226, 298	431, 540
Women				
% (95% CI)	5.6 (2.0–14.4)	2.3 (0.8–6.1)	0.4 (0.1–1.5)	1.7 (0.9–3.3)
UWT, WT denominator	96, 72	166, 158	353, 274	615, 504
Both				
% (95% CI)	4.5 (2.0–9.7)	1.1 (0.4–3.0)	0.2 (0.0–0.7)	1.1 (0.6–1.9)
UWT, WT denominator	163, 148	304, 324	579, 572	1,046, 1,044

^a one-sided binomial 97.5% confidence interval.

CI = confidence interval, UWT = unweighted count of individuals, WT = weighted count of individuals.

Table 2 | Association of sexually transmitted infection with *Chlamydia trachomatis* with selected sexual behavior characteristics among sexually experienced individuals 18 to 24 years old, Slovenia, 2016–2017.

Value	Prevalence % (95% CI)	UWT, WT denominator	OR	95% CI	AOR	95% CI
≥ 1 new heterosexual partner in past year						
No	1.1 (0.2–7.2)	123, 111	1	–	1	–
Yes	19.9 (9.0–38.4)	28, 27	23.1	2.6–205.2	13.3 ^a	1.0–171.5
Heterosexual partners in past year						
0–1	1.3 (0.2–8.6)	105, 92	1	–		
2	4.4 (0.6–25.6)	31, 30	3.5	0.2–59.1		
≥ 3	17.4 (6.6–38.4)	24, 24	16.1	1.7–155.3		
Heterosexual partners without consistent condom use in past year						
0–1	2.3 (0.6–8.3)	133, 121	1	–	1	–
≥ 2	21.1 (6.8–49.5)	17, 16	11.6	1.7–77.2	7.7 ^b	1.3–45.5
≥ 10 heterosexual partners in lifetime						
No	3.1 (1.0–8.9)	144, 131	1	–		
Yes	17.7 (5.2–45.6)	16, 15	6.8	1.2–40.0		
Ever had same-sex experience						
No	3.6 (1.4–8.7)	153, 141	1	–	1	–
Yes	19.7 (4.4–56.8)	10, 8	6.6	0.9–46.2	13.5 ^c	1.0–177.9

^a Adjusted for number of heterosexual partners without consistent (100%) condom use in the past year and ever had same-sex experience.

^b Adjusted for ≥ 1 new heterosexual partner in the past year and ever had same-sex experience.

^c Adjusted for number of heterosexual partners without consistent (100%) condom use in the past year and ≥ 1 new heterosexual partner in the past year.

Only 146 records with complete data for all variables were used in the final multivariate logistic regression model. Only variables with $p < 0.1$ were included in explorative multivariate logistic regression models.

AOR = adjusted odds ratio, CI = confidence interval, OR = odds ratio, UWT = unweighted count of individuals, WT = weighted count of individuals.

Table 3 | Association of sexually transmitted infection with *Chlamydia trachomatis* with selected sexual behavior characteristics among sexually experienced women 18 to 49 years old, Slovenia, 2016–2017.

	Prevalence % (95% CI)	UWT, WT denominator	OR	95% CI	AOR	95% CI
Age group						
18–24	5.6 (2.0–14.4)	96, 72	($p = 0.01$) 15.3	2.7–87.7	($p = 0.08$) 8.9 ^a	1.3–59.1
25–34	2.3 (0.8–6.1)	166, 158	6.0	1.1–34.4	3.9 ^a	0.6–26.7
35–49	0.4 (0.1–1.5)	353, 274	1	–	1	–
≥ 1 new heterosexual partner in past year						
No	1.0 (0.5–2.4)	533, 442	($p < 0.01$) 1	–	($p < 0.01$) 1	–
Yes	21.0 (9.8–39.6)	23, 19	25.4	7.4–86.7	8.9 ^b	2.5–31.9
First sex before age 16						
No	1.3 (0.6–2.8)	525, 431	($p = 0.05$) 1	–	–	–
Yes	5.1 (1.6–14.9)	77, 63	4.3	1.0–18.0	–	–
≥ 10 heterosexual partners lifetime						
No	1.2 (0.5–2.8)	524, 428	($p = 0.14$) 1	–	–	–
Yes	3.7 (1.1–11.5)	73, 64	3.1	0.7–14.1	–	–
Number of heterosexual partners in past year						
0–1	1.1 (0.5–2.4)	535, 438	($p = 0.02$) 1	–	–	–
≥ 2	5.6 (1.8–16.3)	60, 51	5.6	–	–	–
Ever had same-sex experience						
No	1.5 (0.7–3.0)	581, 475	($p = 0.22$) 1	–	–	–
Yes	5.5 (0.8–30.3)	32, 28	3.9	0.5–33.2	–	–
Ever received payment for sex						
No	1.4 (0.7–2.9)	604, 495	($p < 0.01$) 1	–	($p < 0.01$) 1	–
Yes	51.3 (11.8–89.3)	4, 3	73.6	8.1–666.6	72.9 ^c	12.4–430.0

^a Adjusted for ≥ 1 new heterosexual partner in the past year and ever received payment for sex.

^b Adjusted for age group and ever received payment for sex.

^c Adjusted for age group and ≥ 1 new heterosexual partner in the past year.

Only 551 records with complete data for all variables were used in the final multivariate logistic regression model. Only variables with $p < 0.1$ were included in explorative multivariate logistic regression models.

AOR = adjusted odds ratio, CI = confidence interval, OR = odds ratio, UWT = unweighted count of individuals, WT = weighted count of individuals.

al behavior characteristics among sexually experienced women 18 to 49 years old. The prevalence of CT infection was 21 times higher among those that reported at least one new heterosexual partner in the past year in comparison to others ($p < 0.01$), four times higher among those that had their first heterosexual intercourse before age 16 in comparison to others ($p = 0.05$), five times higher among those that reported two or more heterosexual partners in the past year in comparison to others ($p = 0.02$), and 37 times higher among those that had ever received payment for sex in comparison to those that had not ($p < 0.01$).

In multivariate analysis, women with at least one new heterosexual partner in the past year had nine times higher odds of CT infection (AOR: 8.9; 95% CI: 2.5–31.9; $p < 0.01$), and those reporting to have ever received payment for sex had 73 times higher odds of CT infection (AOR: 72.9; 95% CI: 12.4–430.0; $p < 0.01$). Limiting the analysis to sexually experienced 25- to 49-year-old women, reporting at least one new heterosexual partner in the past year was associated with having CT infection in the bivariate model (AOR: 11.2; 95% CI: 1.2–109.2; $p = 0.04$). In the multivariate model, only receiving payment for sex remained statistically significant (AOR: 116.2; 95% CI: 13.0–1035.9; $p < 0.01$).

Discussion

Our results show that the prevalence of CT infection was rather high among sexually experienced individuals under 25 residing in Slovenia in 2016 and 2017. It was higher among women than men,

and particularly high among women 18 to 24 years old. Having a new heterosexual partner in the past year was identified as a risk factor for CT infection among women of all ages surveyed (18–49 years) as well as among 18- to 24-year-olds. Other sexual behavior risk factors for CT infection identified in our analyses were generally in line with risk factors identified in other studies and reflected in the testing guidelines of many developed countries (13–17, 20). Approximately three-quarters of women of all ages surveyed as well those 18 to 24 years old reported at least one visit to a gynecologist as part of primary healthcare services during the past year.

In contrast to our survey results, only having five or more lifetime heterosexual partners was identified as a risk factor for CT infection among sexually experienced 18- to 24-year-olds in the first Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 1999–2000 (10).

Due to the very similar methodology, our results are most comparable to the third British National Survey of Sexual Attitudes and Lifestyles (Natsal-3) (20). That study also used a general population probability sample, although with a slightly different age range (16–44 years). Similar to our results, British women of increasingly older age groups had significantly decreasing adjusted odds for genital CT infection compared to women 16 to 19 years old. In Natsal-3, reporting two or more sexual partners without consistent condom use in the past year was found to be a significant predictor for CT infection among British women 16 to 44 years old. In addition, most socially deprived British women had significantly higher adjusted odds of genital CT infection. Our

small sample size (1,046 persons with CT test results and 12 cases of CT infection) in comparison to the Natsal-3 sample size (4,550 persons with CT test results and 98 cases of CT infection) prevented us from having enough cases to explore potential covariates present in small proportions in the study population.

Based on the high estimated prevalence of CT infection among young sexually active women in Slovenia, we propose considering the introduction of annual opportunistic CT testing for sexually active women under 25, which is in line with numerous national and international guidelines for CT infection control (13–17). Because a majority of sexually experienced 18- to 24-year-old women reported having visited a gynecologist in the previous year, testing should first be implemented in the primary healthcare outpatient gynecology services that perform sexual and reproductive health services for women in Slovenia. Early detection of CT infections and timely treatment would prevent numerous long-term complications for reproductive health. Based on risk factor analysis, offering chlamydia testing to sexually active women 25 years or older with a new heterosexual partner in the preceding year in the primary healthcare outpatient gynecology services should also be considered. Among sexually experienced women 25 to 49 years old, a majority also reported having visited a gynecologist in the previous year. Screening of older women at increased risk of infection (e.g., those that have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner that has a STI) has been recommended by the United States Centers for Disease Control and Prevention (15). Partner change in the last 12 months is also a specific clinical indicator for CT infection testing in Australian STI management guidelines for primary care (17).

In addition to such opportunistic testing, there should also be continuation of evidence-based case management, including partner notification, as well as sexual and reproductive health education and promotion of condom use as part of wider primary STI prevention, especially among and together with young people (2, 14). Effectiveness of partner notification and treatment, when needed, is essential because inadequately treated partners can reintroduce CT infection into an ongoing sexual partnership or can leave other partners in a sexual network untreated (22). Repeated infection can also result from a new partner or antibiotic treatment failure; all of the guidelines mentioned above recommend retesting of diagnosed cases within 3 to 6 months (13–17). Individual follow-up varies. Performing test-of-cure using nucleic acid amplification tests is recommended 4 weeks after completion of therapy in specific circumstances: that is, in pregnancy, in complicated infections, in extra-genital infections, if symptoms persist, if second-line or third-line treatment regimens have been used, and if non-compliance to therapy or re-exposure of infection is suspected (14). Because receiving payment for sex was a strong predictor of CT infection, reaching high-risk population groups such as commercial sex workers to ensure their access to regular testing should also be considered.

Although many European countries reported having guidelines for opportunistic CT testing of specific population groups (23), the need for cautious evaluation of the benefit-to-harm ratio and the cost-effectiveness of widespread testing for asymptomatic CT infections in high-income countries has recently been raised (2, 22, 24, 25). There is moderate quality evidence from randomized controlled trials that testing asymptomatic women reduces the risk of pelvic inflammatory disease, an intermediate endpoint of reproductive tract damage in women. However, there

is uncertainty about how lower testing uptake would affect this reduction and whether widespread testing reduces long-term complications such as tubal factor infertility. Mathematical models have suggested that population-based screening could reduce the prevalence (2, 26). However, there is no convincing practice-based evidence that widespread opportunistic testing, particularly if uptake levels are low or decreasing, would reduce the CT infection prevalence. Concerns were also raised that widespread testing may result in overdiagnosis and overtreatment, and may contribute to increased antimicrobial resistance to other STI and non-STI pathogens as well as to psychological and social harm. Most cost-effectiveness studies in high-income countries have concluded that at least one strategy for CT screening was cost-effective at nationally accepted thresholds; however, assumptions about model structure and about the probability of complications of the infection in several studies tended to favor screening (22, 27, 28). For these reasons, the ECDC recommended widespread opportunistic testing or screening programs for sexually active men and women under 25 only if sufficient resources are available and suitable monitoring and evaluation is in place (2). Considering currently available evidence, Dutch experts recommended targeted testing combined with effective case management and primary prevention instead of screening and widespread testing in the Netherlands, and widespread register-based chlamydia screening with low levels of uptake was discontinued (25). External peer review of evidence for the National Chlamydia Screening Programme in England also concluded that detecting and treating CT infections can prevent subsequent harm in asymptomatic women, but that there is no strong empirical evidence that screening of women and men has resulted in a fall in CT infection prevalence. Prevention of harm from sequelae of CT infection in women was recommended as a primary aim of the program rather than prevention of ongoing transmission and reducing infection in the overall population. The National Chlamydia Screening Programme in England, which used to recommend opportunistic screening for sexually active men and women under 25, has focused only on sexually active women under 25 since June 2021 (13). Thus, our proposal—introducing annual opportunistic CT testing for sexually active women under 25 and offering chlamydia testing to sexually active women 25 years and older with a new heterosexual partner in the preceding year within the primary healthcare outpatient gynecology services with quite good coverage of the target population—is in line with most recent recommendations on targeted testing, case management, and primary prevention of CT infection (2, 13–17, 25).

CT serovars L1, L2, and L3 cause lymphogranuloma venereum (LGV), a systemic STI reported to occur among the population of European men that have sex with men (MSM) since 2003 (29, 30). In our study, we did not further test CT-positive samples for LGV serovars. It is worth noting that neither of the two men infected with CT had homosexual experience.

Strengths of the second Slovenian National Survey of Sexual Lifestyles, Attitudes, and Health in 2016–2017 include using a national probability sample of the general population from a reliable sampling frame and an acceptable 55.5% survey response rate as well as the 57.0% urine specimen collection rate among survey respondents. It should be noted that the urine specimen testing rate among eligible individuals was only 31.3%. However, the survey response and urine specimen collection rates were quite similar to the overall response (57.7%) and urine specimen collection rate (60.0%) in the British Natsal-3 (20). To minimize non-participation bias, the sample of respondents that provided urine speci-

mens was weighted to match the distribution of sex, age, region, and size and type of community of the general population. One of the limitations of our survey was the small sample size. Thus, our estimations of the prevalence of CT infection among different age groups of men and women were less precise than desired, and we lacked the power for exploratory analyses for risk factors within narrower age groups. Despite minimizing participation bias by weighting, respondents providing urine specimens may not have been fully representative of the sexually experienced general population of 18- to 49-year-olds. Some participation bias could be present if sexual behavior and sexual risk differed between respondents and non-respondents as well as between those that provided a urine specimen and those that did not. For example, groups that tend to be stigmatized such as commercial sex workers may have been underrepresented. Detection of CT infections could have lower sensitivity in women because of using first-void urine specimens for testing. This might detect up to 10% fewer infections when compared with vaginal and endocervical swab samples. In men, a first-void urine specimen is equivalent to a urethral swab. Consequently, an optimal vaginal swab and first-void urine are the recommended sample types for detecting CT infection in women and men, respectively. However, first-void urine in women is acceptable for screening (31). Sensitivity of the PCR assay might also differ depending on the procedure by which the urine sample is collected. First-void urine allows the detection of infected epithelial cells and associated CT particles. The use of FirstBurst improves the sensitivity for detecting CT infection over testing of samples collected with a urine cup (19). Finally, other limitations included validity constraints of self-reported information about sexual behavior that are inherent in all such surveys.

Based on our results and on the most recent other national and international recommendations for CT infection management, we conclude that, because of the high prevalence of CT infection among 18- to 24-year-old women living in Slovenia and the risk

of long-term reproductive effects, opportunistic testing of sexually active women under age 25 should be considered. In addition, offering testing for CT infection to older women with a new sexual partner in the past year should also be considered. This should be implemented first in primary healthcare outpatient gynecology services that perform sexual and reproductive health services for women in Slovenia.

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References

- Rowley J, Vander Hoorn S, Korenromp E, Low N, Unemo M, Abu-Raddad LJ, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. *Bull World Health Organ.* 2019;97:548–62P.
- European Centre for Disease Prevention and Control. Guidance on chlamydia control in Europe, 2015 [Internet]. ECDC; 2016 [cited 2021 Aug 15]. Available from: <https://data.europa.eu/doi/10.2900/667703>.
- Henkel R. Long-term consequences of sexually transmitted infections on men's sexual function: a systematic review. *Arab J Urol.* 2021;19:411–8.
- Videčnik Zorman J, Matičič M, Jevec S, Smrkolj T. Diagnosis and treatment of bacterial prostatitis. *Acta Dermatovenerol Alp Pannonica Adriat.* 2015;24:25–9.
- Huai P, Li F, Chu T, Liu D, Liu J, Zhang F. Prevalence of genital *Chlamydia trachomatis* infection in the general population: a meta-analysis. *BMC Infect Dis.* 2020;20:589.
- World Health Organization. Global health sector strategy on sexually transmitted infections, 2016–2021 [Internet]. WHO; [cited 2021 Aug 15]. Available from: <https://www.who.int/reproductivehealth/publications/rtis/ghss-stis/en/>.
- Nacionalni inštitut za javno zdravje (NIJZ). Spolno prenesene okužbe v Sloveniji. Letno poročilo 2018. [Internet]. NIJZ; 2019 [cited 2021 Aug 15]. Available from: <https://www.nijz.si/sl/epidemiolosko-spremljanje-nalezljivih-bolezni-letna-in-cetrletna-porocila>.
- European Centre for Disease Prevention and Control. Chlamydia infection. Annual epidemiological report for 2018 [Internet]. ECDC; 2020 [cited 2021 Aug 15]. Available from: <https://www.ecdc.europa.eu/sites/default/files/documents/AER-for-2018-STI-chlamydia.pdf>.
- Kustec T, Keše D, Klavs I. Under-reporting of sexually transmitted infection with *Chlamydia trachomatis*—a revision of surveillance system is required. *Slov J Public Health.* 2016;55:174–8.
- Klavs I, Rodrigues LC, Wellings K, Keše D, Hayes R. Prevalence of genital *Chlamydia trachomatis* infection in the general population of Slovenia: serious gaps in control. *Sex Transm Infect.* 2004;80:121–3.
- Mihevč Ponikvar B, Krotec I, Klavs I. Spolno prenosljive okužbe z bakterijo *Chlamydia trachomatis* v Sloveniji. *Slov J Public Health.* 2013;52:59–68.
- Cassini A, Colzani E, Pini A, Mangan MJ, Plass D, McDonald SA, et al. Impact of infectious diseases on population health using incidence-based disability-adjusted life years (DALYs): results from the Burden of Communicable Diseases in Europe study, European Union and European Economic Area countries, 2009 to 2013. *Eurosurveillance.* 2018;23:17.
- Public Health England. National Chlamydia Screening Programme (NCSP): programme overview [Internet]. GOV.UK. [cited 2021 Aug 15]. Available from: <https://www.gov.uk/government/publications/ncsp-programme-overview/ncsp-programme-overview>.
- Lanjouw E, Ouburg S, de Vries H, Stary A, Radcliffe K, Unemo M. 2015 European guideline on the management of *Chlamydia trachomatis* infections. *Int J STD AIDS.* 2016;27:333–48.
- Centers for Disease Control and Prevention. STI screening recommendations [Internet]. CDC; 2021 [cited 2021 Aug 15]. Available from: <https://www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm>.
- Public Health Agency of Canada. Chlamydia and LGV: key information and resources [Internet]. Government of Canada; 2020 [cited 2021 Aug 15]. Available from: <https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/chlamydia-lgv.html>.

17. Australasian Sexual Health Alliance. Chlamydia—Australian STI management guidelines [Internet]. ASHA. [cited 2021 Aug 15]. Available from: <http://www.sti.guidelines.org.au/sexually-transmissible-infections/chlamydia#diagnosis>.
18. Klavs I, Milavec M, Berlot L, Kustec T, Grgič-Vitek M, Lavtar D, et al. Prevalence of sexually transmitted infections with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and *Trichomonas vaginalis*: findings from the Slovenian National Survey of Sexual Lifestyles, Attitudes and Health, 2016–2017. *Eurosurveillance*. 2021. In press.
19. Wisniewski CA, White JA, Michel CE, Mahilum-Tapay L, Magbanua JP, Nadala EC Jr, et al. Optimal method of collection of first-void urine for diagnosis of *Chlamydia trachomatis* infection in men. *J Clin Microbiol*. 2008;46:1466–9.
20. Sonnenberg P, Clifton S, Beddows S, Field N, Soldan K, Tanton C, et al. Prevalence, risk factors, and uptake of interventions for sexually transmitted infections in Britain: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *Lancet*. 2013;382:1795–806.
21. Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections—management and treatment of specific infections—chlamydial infections [Internet]. Government of Canada; 2013 [cited 2021 Aug 15]. Available from: <https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections-30.html>.
22. European Centre for Disease Prevention and Control. Chlamydia control in Europe: literature review. [Internet]. ECDC; 2014 [cited 2021 Aug 15]. Available from: <https://data.europa.eu/doi/10.2900/16352>.
23. European Centre for Disease Prevention and Control. Chlamydia control in Europe: a survey of member states, 2012. [Internet]. ECDC; 2014 [cited 2021 Aug 15]. Available from: <https://data.europa.eu/doi/10.2900/30120>.
24. Low N, Redmond S, Uusküla A, Bergen J van, Ward H, Andersen B, et al. Screening for genital chlamydia infection. *Cochrane Database Syst Rev*. 2016;9:CD010866.
25. Bergen JEAM van, Hoenderboom BM, David S, Deug F, Heijne JCM, Aar F van, et al. Where to go to in chlamydia control? From infection control towards infectious disease control. *Sex Transm Infect*. 2021;97:501–6.
26. Rönn MM, Tuite AR, Menzies NA, Wolf EE, Gift TL, Chesson HW, et al. The impact of screening and partner notification on chlamydia prevalence and numbers of infections averted in the United States, 2000–2015: evaluation of epidemiologic trends using a pair-formation transmission model. *Am J Epidemiol*. 2019;188:545–54.
27. Rönn MM, Wolf EE, Chesson H, Menzies NA, Galer K, Gorwitz R, et al. The use of mathematical models of chlamydia transmission to address public health policy questions: a systematic review. *Sex Transm Dis*. 2017;44:278–83.
28. Wang LY, Owusu-Edusei K, Parker JT, Wilson K. Cost-effectiveness of a school-based chlamydia screening program, Duval County, FL. *J Sch Nurs*. 2021;37:195–201.
29. European Centre for Disease Prevention and Control. Facts about lymphogranuloma venereum [Internet]. ECDC; 2016 [cited 2021 Nov 8]. Available from: <https://www.ecdc.europa.eu/en/lymphogranuloma-venereum/facts>.
30. Matičič M, Klavs I, Videčnik Zorman J, Vidmar Vovko D, Kogoj R, Keše D. Confirmed inguinal lymphogranuloma venereum genovar L2c in a man who had sex with men, Slovenia, 2015. *Euro Surveill*. 2016;21:pii=30129.
31. Centers for Disease Control and Prevention. Recommendations for the laboratory-based detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014 [Internet]. CDC; 2014 [cited 2021 Nov 8]. Available from: <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6302a1.htm#Box2>.