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Research

Estimating the test-adjusted incidence of *Chlamydia trachomatis* infections identified through Public Health Ontario Laboratories in Peel region, Ontario, 2010–2018: a population-based study

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Abstract

Background: Public health guidelines for chlamydia testing are not sex specific, but young females test at a disproportionally higher rate than males and other age groups. This study aims to describe testing trends across age and sex subgroups, then estimate a test-adjusted incidence of chlamydia in these subgroups to identify gaps in current testing practices.

Methods: We used a population-based study to examine observed chlamydia rates by age and sex subgroups: 15–19 years, 20–29 years, 30–39 years and older than 40 years. The study included diagnostic test results recorded by Public Health Ontario Laboratories between Jan. 1, 2010, and Dec. 31, 2018, for individuals living in Peel region, Ontario. We then employed meta-regression models as a method of standardization to estimate the effect of sex and age on standardized morbidity ratio, testing ratio and test positivity, then calculate a test-adjusted incidence of chlamydia for each subgroup.

Results: Over the study period, infection, testing and test positivity varied across age and sex subgroups. Observed incidence and testing were highest in females aged 20–29 years, whereas males had the highest standardized test positivity across all age groups. After estimating test-adjusted incidence for each age–sex subgroup, males in the 15–19-year and 30–39-year age groups had an increase in incidence of 60.2% and 9.7%, respectively, compared with the observed incidence.

Interpretation: We found that estimated test-adjusted incidence was higher than observed incidence in males aged 15–19 years and 30–39 years. This suggests that infections in males are likely being missed owing to differential testing, and this may be contributing to the persistent increase in reported cases in Canada. Public health programming that targets males, especially in high-risk settings and communities, and use of innovative partner notification methods could be critical to curbing overall rates of chlamydia.

Public health guidelines for sexually transmitted infection (STI) testing and screening make recommendations regarding the groups of individuals to whom to target testing and screening resources.[1] Screening is a tool used to reduce disease burden, particularly in high-risk groups, and is largely important for STIs where infections can often be asymptomatic. Screening differs from diagnostic testing, in which individuals are tested because they present with symptoms consistent with an STI. In the case of chlamydia, the Public Health Agency of Canada recommends annual screening for sexually active people younger than 25 years; and a recent report from the Canadian Task Force on Preventive Care recommends annual screening for sexually active people younger than 30 years.[1,2] Despite national screening guidelines, many factors determine whether, and how often, individuals get tested. In Canada, 60% of people surveyed reported they had never been screened for STIs, suggesting that even with current guidelines, many patients are not screened routinely for STIs.[3]

Substantial emphasis is placed on testing females younger than 25 years, owing to the often asymptomatic nature of chlamydia infections and the possibility of long-term health complications, including pelvic inflammatory disease, infertility and ectopic pregnancy.[1,4,5] However, screening males has been the subject of substantial debate, and various organizations in the United States, including the Centers for Disease

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Control and Prevention (CDC) and the US Preventive Services Task Force, claim there is insufficient evidence to support regular screening of young men.[6,7] Despite noting that asymptomatic infections are common in both males and females, the CDC does not advise general screening of males for chlamydia and states that it should be considered only in high-risk populations, such as men who have sex with men.[6] In Canada, although guidelines are not sex specific, testing efforts have primarily focused on females younger than 25 years, and rates of chlamydia in this group continue to increase.[8] This leads to questions regarding the factors that may be contributing to this observed increase. Are increased rates simply a function of increased testing and, therefore, improved case finding? Or is a group of individuals (e.g., males or another age group) being missed by current testing practices and thereby contributing to the transmission dynamics but not being identified and receiving treatment to cure their undiagnosed infection? For example, infections in males going undiagnosed can result in an ongoing chain of transmission, so that in heterosexual relationships, female partners are at risk of infection or reinfection.

To better understand the influence of testing rates on case detection rates in populations where not all subgroups are tested at the same intensity, standardization can be used. Standardization can adjust for testing rates among different subgroups of interest to provide an adjusted incidence estimate based on the assumption that all groups were tested at the same rate as the observed maximally tested group.[9] We hypothesize that males would have higher incidence rates if tested at the same rate as females, because males are undertested. This study focused on chlamydia tests analyzed by Public Health Ontario Laboratories (PHOL) for people residing in Peel, Ontario, a regional municipality in the Greater Toronto Area. The objectives of this study were to describe the trends in incidence, tests and test positivity of chlamydia across subgroups over the study period, 2010–2018, in Peel region, Ontario; to determine subgroups that had the highest infection, testing and test positivity rates; and to estimate the test-adjusted incidence of chlamydia in subgroups, assuming they were tested at the same rate as the maximally tested group.

Methods

Study design

This population-based study describes and investigates differential testing for chlamydia across age and sex subgroups for individuals tested between Jan. 1, 2010, and Dec. 31, 2018. We followed the Reporting of Studies Conducted Using Observational Routinely-collected Data (RECORD) Statement checklist when reporting the findings.[10]

Setting and population

We used Peel region, Ontario, as a case study to examine testing trends. Peel is a regional municipality with an estimated population of 1.48 million in 2018.[11] Peel is a unique region in which 2 of the 3 municipalities (Mississauga and Brampton) are large urban cities, and the third (Caledon) is primarily rural. Individuals included in the study were aged 15 years (or older) at the time of testing and had a postal address within the region of Peel, Ontario. To be included in the study, testing for chlamydia must have been completed at 1 of the PHOL locations between Jan. 1, 2010, and Dec. 31, 2018. In Ontario, chlamydia testing is ordered by practitioners and can be analyzed at PHOL, private laboratories or hospital laboratories, funded through the Ontario Health Insurance Plan. Where the specimen is sent for testing depends on the ordering practitioner and setting — for example, specimens collected at public health clinics are sent to PHOL.

Data sources

During the study period, nucleic acid amplification tests were the recommended testing method for chlamydia at PHOL.[12] Results indicating a positive chlamydia test, from all laboratories, must be reported through the integrated Public Health Information System in Ontario, which we used as the data source for cases.[13] We then subset the cases by reporting laboratory to include only those completed by PHOL, then calculated the proportion of cases resulted at PHOL with all cases as the denominator. We obtained the number of tests completed from the Ontario Laboratories Information System (OLIS), an online repository for laboratory test orders and results.[14] The data sets from OLIS and the integrated Public Health Information System obtained for this study do not provide an indicator to determine whether the test was done for screening or diagnostic purposes. We aggregated testing data from OLIS into 10-year age bands, to ensure data privacy, except for ages 15–19 years. To calculate rates, we obtained population estimates from the Statistics Canada 2006, 2011 and 2016 Census profiles.[15–17] We used linear interpolation and extrapolation to estimate non-Census-year population sizes. We used the 2006 and 2011 Census populations to estimate the 2010 population and the 2011 and 2016 Census populations to estimate the 2012–2015 and 2017–2018 populations. For the purpose of the study, we divided the data sets into age–sex subgroups as follows: age 15–19 years, 20–29 years, 30–39 years, and 40 years and older, for males, females and the overall population. Given low testing rates and case counts in individuals aged 40 years or older, we aggregated all age groups older than 40 years into a single group.

Statistical analysis

We conducted descriptive analysis of testing rates, incidence and test positivity to examine trends in the data and to determine our maximally tested subgroup for further analyses. We estimated standardized morbidity ratio (SMR), standardized testing ratio (STR) and standardized test positivity (STP) for monthly and cumulative data to explore infections, testing and test positivity. A ratio greater than 1 indicates that infections, testing or test positivity are higher than expected, and less than 1 indicates they are lower than expected. We calculated average annual incidence of infection, testing and positivity per test for the population as a whole and for each age–sex

subgroup, then calculated ratio estimates. We then used meta-regression models to explore the effects of age and sex on SMR, STR and STP (Appendix 1, EQ2, available at www.cmajopen.ca/content/11/1/E62/suppl/DC1).

To account for the differential testing across age and sex subgroups, we applied a test-adjusted incidence using standardization. First, we estimated the "test-adjusted" SMR for each age–sex subgroup using meta-regression models (Appendix 1, EQ3). To investigate this further, we calculated the expected test frequency–adjusted incidence of each subgroup (if tested at the same rate as the maximally tested subgroup) (Appendix 1, EQ4). This calculation was conducted for each age–sex subgroup, where females aged 20–29 years were the maximally tested subgroup. To determine whether there was a change in incidence after test-frequency adjustment, we compared test-adjusted incidence with observed incidence. If the observed incidence was outside of the 95% confidence interval of the test-adjusted incidence, we determined that it was of interest and calculated the relative difference.

We conducted all analyses using StataIC 16. We created figures using the ggplot2 package in R-4.0.2 and RStudio. We used a significance level of 5% for all tests and confidence intervals.

Ethics approval

This study was approved by the University of Guelph Research Ethics Board (REB No. 18-11-001).

Results

Study setting and participants

The data set included 10 298 cases and 186 567 tests reported by PHOL in Peel, Ontario, between Jan. 1, 2010, and Dec. 31, 2018. This accounted for 32% of all chlamydia cases identified in Peel region within the study period, determined proportion completed through PHOL compared with total cases identified through all sources. We removed individuals with unknown age (0 cases, 16 tests) and unknown sex (21 cases, 3210 tests), resulting in a final data set of 10 277 cases and 183 341 tests.

Testing trends

Incidence, testing rate and test positivity ranged across age and sex groups over time (Figure 1; Appendix 1, Table A2). Case incidence in the 15- to 19-year and 20- to 29-year age groups among females were the highest throughout the study period and remained above 300 cases per 100 000 for most of

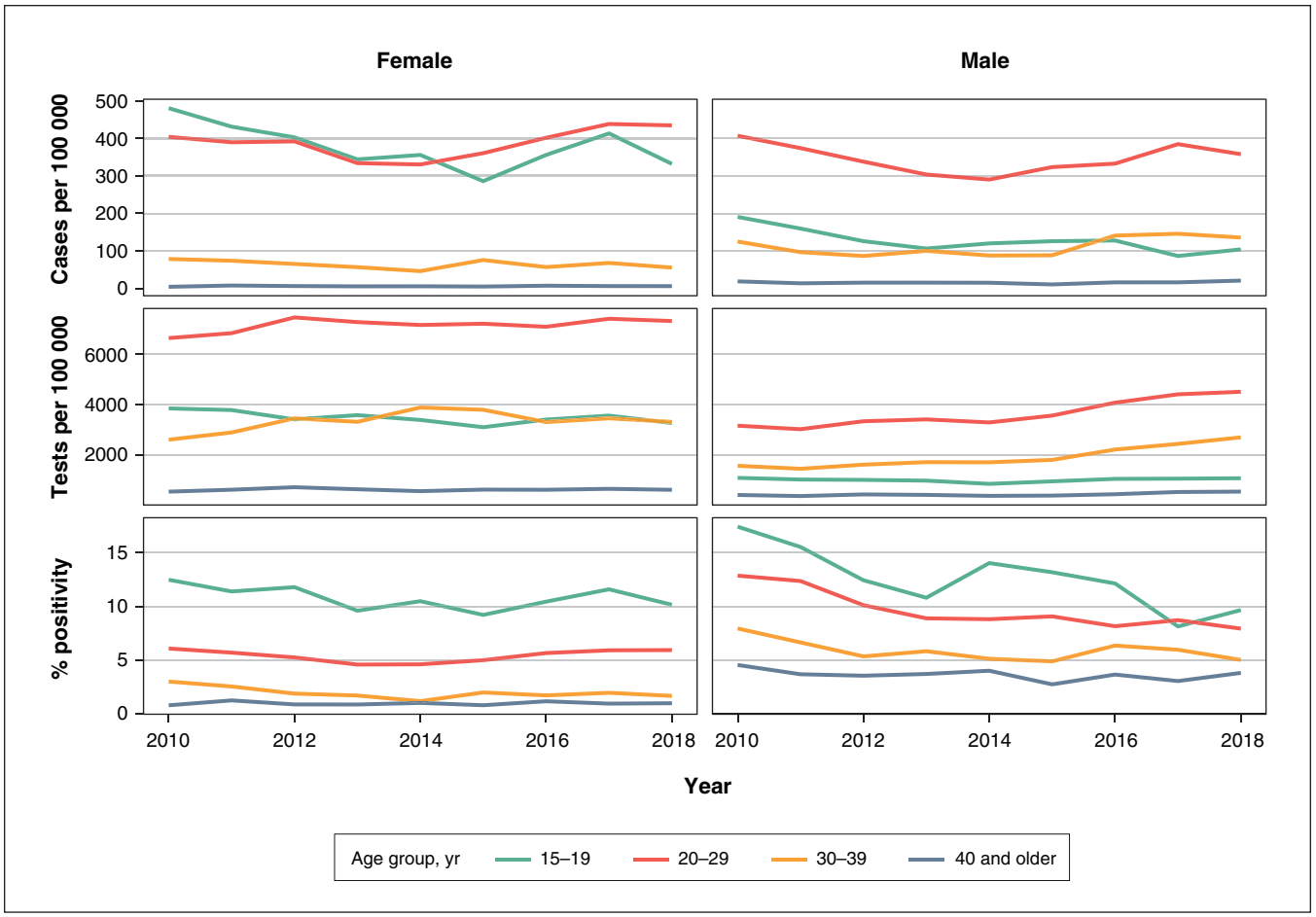

Figure 1: Line graphs of annual chlamydia cases and tests per 100000 population (top 2 panels in each column) and test positivity (bottom panel in each column), grouped by sex and age, in Peel, Ontario, identified through Public Health Ontario Laboratories, 2010–2018.

the study period. In males, the 20- to 29-year age group had consistently higher incidence than all other male age groups, ranging from 291 cases per 100 000 to 408 cases per 100 000. With regard to testing, the 20- to 29-year age group was the most tested per 100 000 population in both sexes. However, the rate of testing was much higher in females at about 7000 tests per 100 000 population throughout the study period, while in males, this ranged from about 3000 tests per 100 000 in 2010 to 4500 tests per 100 000 population in 2018. Percent test positivity was highest among the 15- to 19-year and 20- to 29-year age groups in both sexes throughout the study period. Percent positivity was generally higher in males, when we compared the same age groups. We examined the average annual incidence across the age groups by sex (Figure 2). The 15- to 19-year and 20- to 29-year age groups had the highest average annual incidence, and females had higher incidence than males. This was reversed in the 30- to 39-year and 40-year-and-older age groups, in which males had higher average annual incidence.

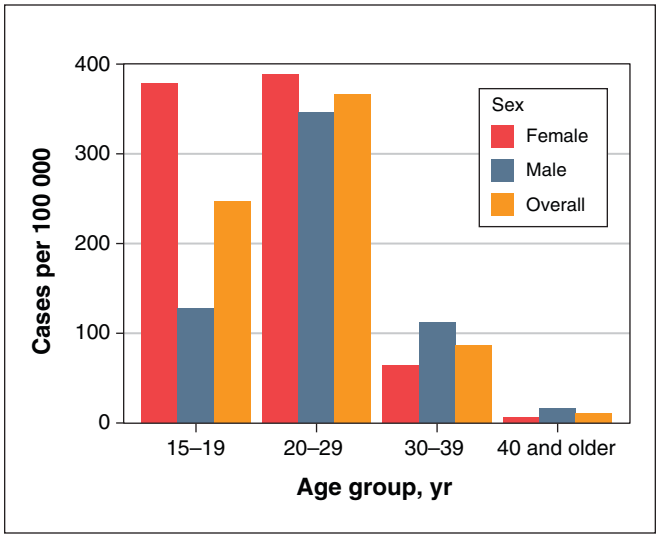

Figure 2: Bar graph of average annual incidence of chlamydia, grouped by age and sex, in Peel, Ontario, identified through Public Health Ontario Laboratories, 2010–2018.

Standardized morbidity, testing and test positivity

The SMR was greater than 1 in females and males aged 15–19 years and 20–29 years, and in 30- to 39-year-old males (Figure 3; Appendix 1, Table A3). The SMR was less than 1 for females aged 30 and older, and in males aged 40 and older (Figure 3; Appendix 1, Table A3). The STR was higher than 1 for females younger than 40 years and males aged 20–29 and 30–39 years (Figure 3; Appendix 1, Table A3). The STR was less than 1 for females and males aged 40 years and older, and in males aged 15–19 years (Figure 3; Appendix 1, Table A3). The STP was greater than 1 in females and males aged 15–19 years, and in males aged 20–29 and 30–39 years (Figure 3; Appendix 1, Table A3). To investigate these trends further, we employed meta-regression models as described in Appendix 1, Table A4.

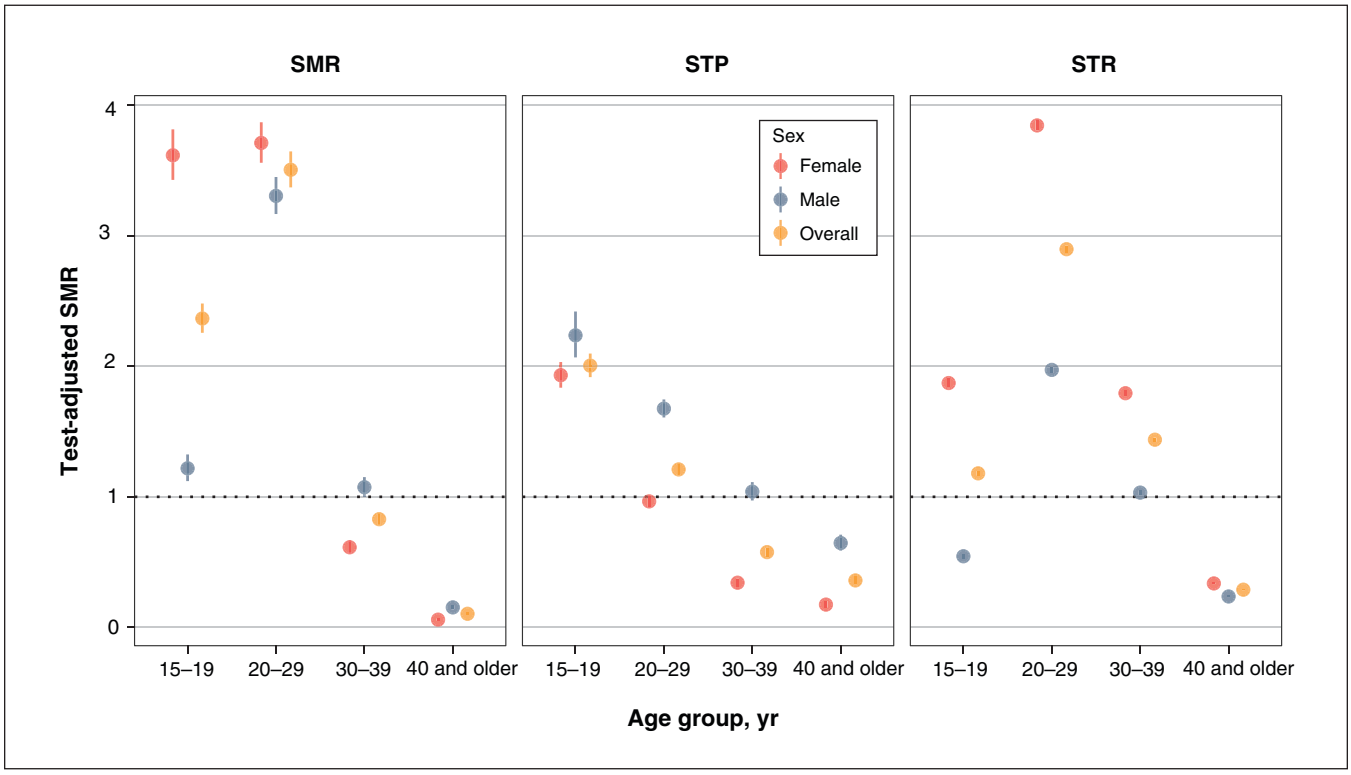

Figure 3: Standardized morbidity ratio (SMR), test positivity (STP) and testing ratio (STR) of chlamydia infections in Peel, Ontario, identified through Public Health Ontario Laboratories, 2010–2018, by sex and age subgroups. The circle indicates the point estimate of SMR, STP or STR; line indicates 95% confidence interval.

Meta-regression models and estimates of test-adjusted incidence

We determined test-adjusted SMR for each age and sex subgroup (Figure 4). Test-adjusted SMR was greater than 1 in males aged 15–19, 20–29 and 30–39 years. In females and the overall population, test-adjusted SMR was greater than 1 in ages 15–19 and 20–29 years. Additionally, the 30- to 39-year age group overall had an SMR greater than 1 but contained 1 in the confidence interval. All other subgroups, females aged 30–29 years and all sexes 40 years and older had a test-adjusted SMR lower than 1.

The most frequently tested age–sex group was females aged 20–29 years (STR = 3.85), and therefore we used the average annual incidence of this group to derive test-adjusted incidence for all other subgroups (Figure 5; Appendix 1, Table A5). The estimated test-adjusted incidence in the population overall, I_0, was 114 cases per 100 000 population. This is an 8.5% increase compared with the observed average annual incidence of 105 cases per 100 000 population. When we compared the test-adjusted incidence with the observed incidence, males aged 15–19 years showed a 60.2% increase and males aged 30–39 years showed a 9.7% increase. The overall incidence in the 30- to 39-year age group was 35.6% higher than the observed incidence after we adjusted for testing. The overall incidence in the 40-year-and-older age group showed a decrease from 11 cases per 100 000 to 6 cases per 100 000 after we adjusted for testing. The test-adjusted incidence in 15- to 19-year-old females, 20- to 29-year-old males and the 20- to 29-year age groups overall showed decreases, but the observed incidence was within the 95% confidence interval of the test-adjusted incidence and deemed to be not different.

Interpretation

This study found that chlamydia incidence in Peel region followed national trends in which females and younger age groups have higher rates of cases.[18] However, after adjusting for differential testing, we found increases in average annual incidence across various age groups, particularly in males. Males were most likely to test positive for chlamydia but had the lowest testing rate, across all age groups (Figure 3). After we adjusted for testing frequency, males in the 15- to 19-year and 30- to 39-year age groups showed an increase of 60.2% and 9.7%, respectively, in average annual incidence of chlamydia when compared with the observed rates (Figure 5). The 30- to 39-year age group showed a 35.6% increase in average annual incidence after adjusting for testing compared with observed rates when we examined both sexes together (Figure 5). These increases, after we adjusted for testing frequency, suggest that these groups may be undertested and that they may play a larger role in the transmission dynamics of chlamydia infections than previously considered.

In this study, year did not have an effect on meta-regression models despite changes to public health policy over time. This could be partially a result of the study data source. This study

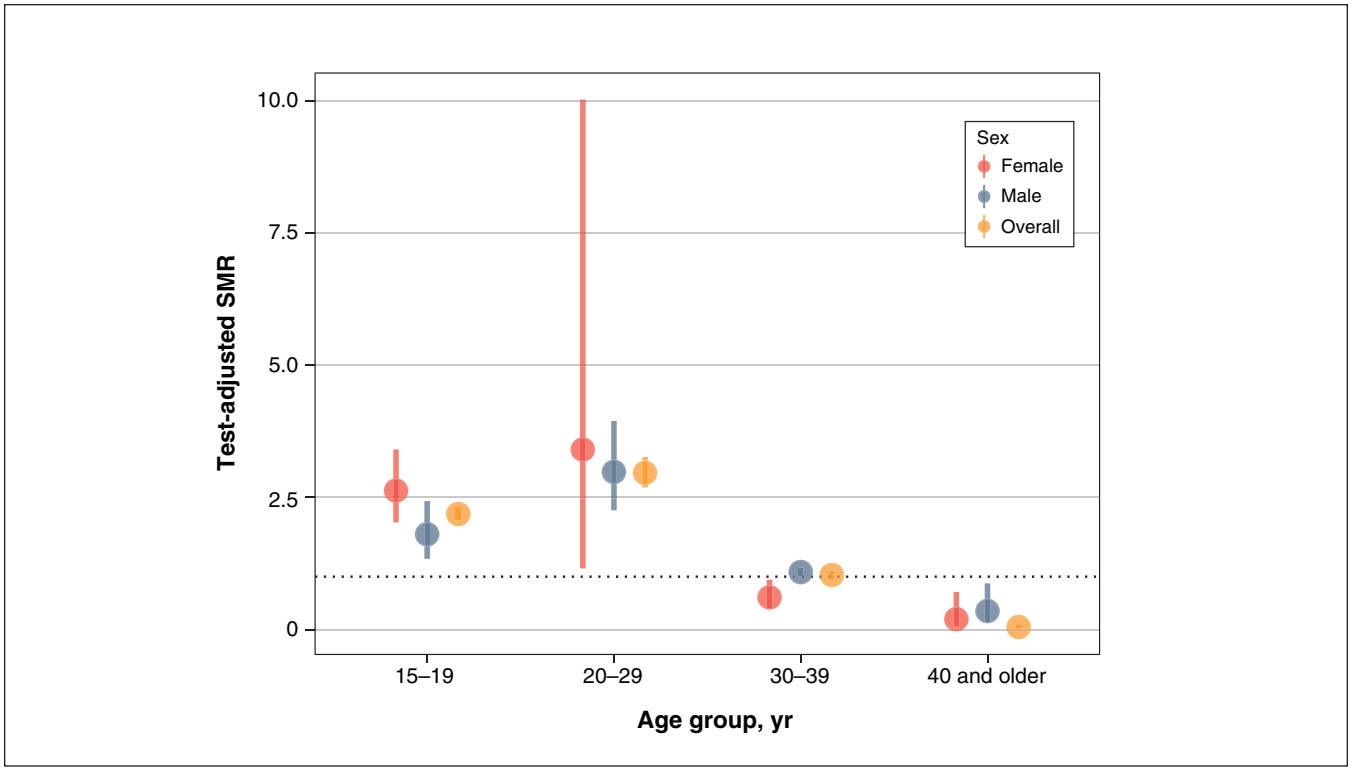

Figure 4: Test-adjusted standardized morbidity ratio (SMR) of chlamydia infections, by age and sex subgroups, in Peel, Ontario, identified through Public Health Ontario Laboratories, 2010–2018. The centre of the circle indicates the point estimate of test-adjusted SMR; line indicates the 95% confidence interval.

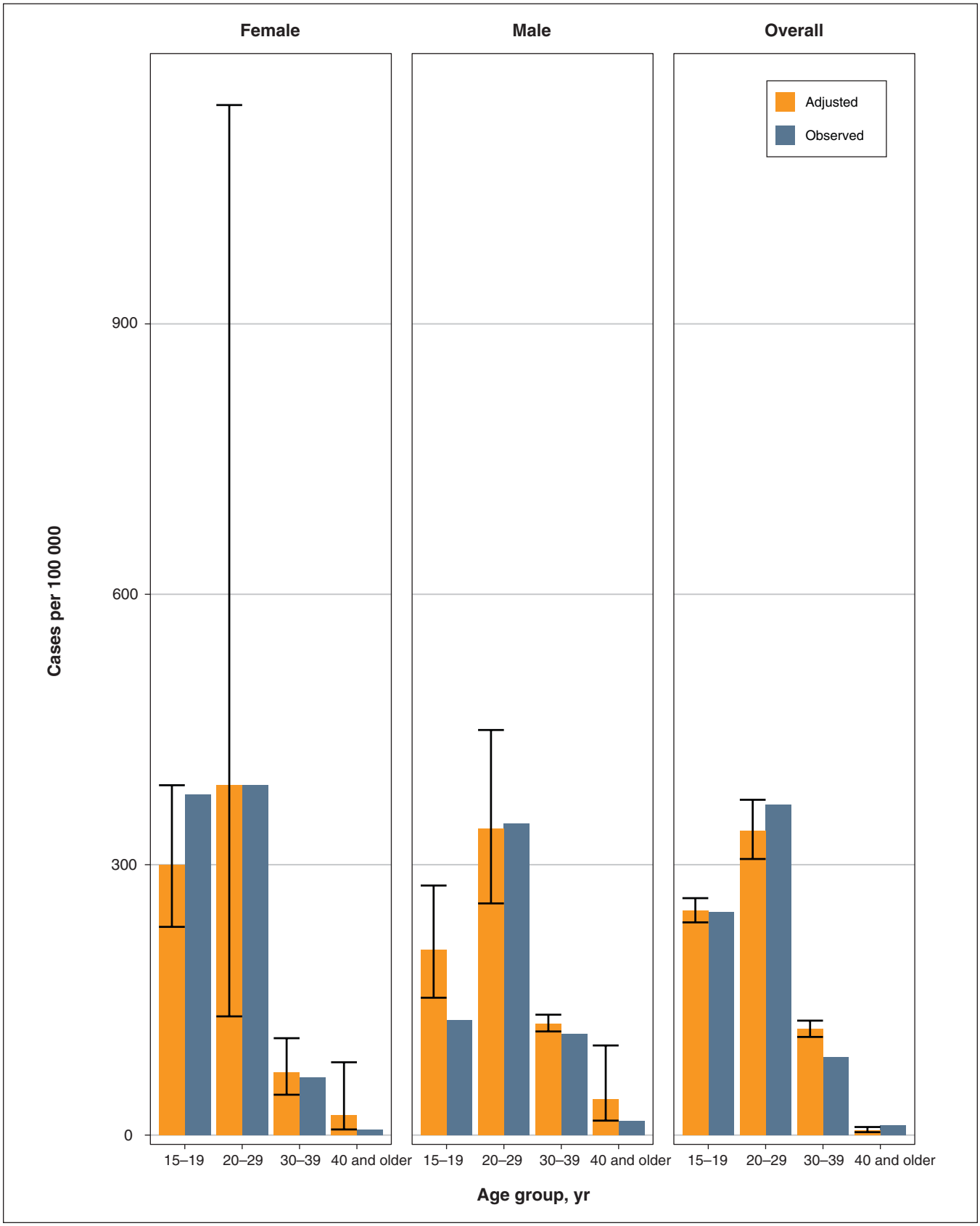

Figure 5: Bar graph of observed and test-adjusted incidence of chlamydia infections, by age and sex subgroups, in Peel, Ontario, identified through Public Health Ontario Laboratories, 2010–2018. Error bars indicate 95% confidence interval of test-adjusted incidence estimates.

used only public health laboratory testing data, which focus primarily on tests performed at public health clinics. In Ontario, a large proportion of STI testing is completed at private laboratories and these data were not accessible for the study. Individuals tested through private laboratories may represent a population with different risk factors and may be screened differently owing to variability in STI screening practices across primary care physicians and nurses.[19–21] In specialized public health clinics, individuals are often seeking STI testing as the reason for their visit and may also have longer consults with care providers.[22,23] This may allow for increased opportunistic screening, or a lower threshold for testing in public health clinics compared with primary care, owing to the dynamics across these settings.

The hypothesis that males would have higher observed incidence rates if tested more often is supported by literature that finds males less likely to seek health care and be screened for STIs during health care visits.[24–27] Males are less likely than females to be tested for chlamydia during routine medical exams despite current testing guidelines indicating anyone younger than 25 years is at risk.[3,21,28] Teenaged males, ages 13–18 years, are also less likely to attend sexual health clinics than teenaged females.[23,27,29] This difference can in part be attributed to teenaged females seeking access to contraceptives, but once an individual attends a sexual health clinic, they are likely to return for future sexual health services, providing more opportunities for STI screening and consultations.[23,27,29]

In this study, we found that more cases would be identified in males if testing was increased in this group. Modelling has shown that screening males may be cost-effective and help prevent new cases of chlamydia and pelvic inflammatory disease in females.[30–32] Modelling by Qu and colleagues showed that for each male screened, 0.062 cases in males and 0.204 cases in females were prevented.[31] Modelling also suggests that screening males should target high-risk individuals specifically.[30,31] This could include settings where chlamydia rates are known to be high (such as in secondary and postsecondary schools), males who attend sexual health clinics, or within geographic areas with known clusters of cases.[30]

Age is also associated with health care–seeking behaviour in that younger people — those who would be most at risk for STIs — are less likely to seek health care.[24] This could explain the persistence of chlamydia in the younger (than age 30 yr) population. It also indicates that more innovative solutions may be needed to curb infections if high-risk individuals are not seeking out testing and treatment. Increased communication regarding the nature of infections, risk of long-term sequelae and recommended testing intervals could help younger individuals make more informed choices regarding STI testing. Innovative methods of outreach such as at-home test kits via an Internet and postal mail service, and expedited partner therapy, could help reach these groups.[33–37] Studies have found that individuals who use Internet-based STI testing have a higher rate of repeat testing than individuals who use clinic-based services.[35] This could help increase testing rates in those less likely to seek out health care, including young males.

Limitations

There are several limitations to consider when making conclusions from this study. The largest limitation is that we included only testing data from provincial public health laboratories. In Peel region, about one-third of cases were identified through a PHOL during the study period. When STI testing is completed through primary care physicians, testing is usually completed at a private laboratory, such as LifeLabs or Dynacare, in Ontario, Canada.[38] Tests performed through public health laboratories may be biased toward individuals tested at public health clinics, where individuals are often seeking STI testing. Additionally, we were unable to identify which tests were completed as *screening* versus for *diagnostic* purposes, and therefore could not make any conclusions regarding this in our study. Focusing on Peel, Ontario, as a subset of the Ontario population may not be representative of chlamydia dynamics in other health units. However, the trends of chlamydia rates by age and sex subgroups in this study do follow similar patterns to the provincial and national trends. For these reasons, caution should be used when generalizing outside Peel region and the community that uses public health clinics. Lastly, we used linear interpolation to estimate population for intercensal years, which has the potential to skew reported results if population growth followed a nonlinear pattern, but we believe the effects to be minimal.

Conclusion

The role of males in transmission dynamics of chlamydia requires further investigation and attention. We found that there is differential testing across age and sex subgroups and that while the most testing occurs in groups of females, males were more likely to test positive, when we compared the same age groups across sexes. From test-adjusted incidence, we found that if males were tested at the same rate as 20- to 29-year-old females, teenaged males (age 15–19 yr) and males aged 30–39 years would likely have higher observed average annual rates of chlamydia than are identified through current testing. Innovative programs that target hard-to-reach, high-risk males, specifically those younger than 30 years, could be critical for reducing the overall burden of chlamydia.

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