ORIGINAL ARTICLE

A Nationwide Observational Study of *Chlamydia trachomatis* Infections in Denmark during the COVID-19 Pandemic

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The aim of this study was to determine whether CO-VID-19 restrictions had an impact on *Chlamydia trachomatis* infections compared with 2018 and 2019. A retrospective nationwide observational study was performed using monthly incidences of laboratory-confirmed chlamydia cases and number of tests, obtained from Danish national surveillance data. Testing rates and positivity rates were compared using Poisson and logistic regression. The first Danish COVID-19 lockdown (12 March to 14 April 2020) resulted in a reduction in the number of chlamydia tests performed (rate ratio 0.72, 95% confidence interval 0.71–0.73) and a consequent reduction in the number of laboratory-identified cases (66.5 vs 88.3 per 100,000 population during the same period in 2018 to 2019). This period was followed by a return of testing and test positivity close to the level seen in 2018 to 2019. The second Danish COVID-19 lockdown (17 December to 31 March 2021) resulted in crude incidence rates of laboratory-confirmed chlamydia infection that were similar to the crude incidence rates seen during same period in 2018 to 2019. In conclusion, the Danish COVID-19 restrictions have had negligible effects on laboratory-confirmed *C. trachomatis* transmission.

Key words: chlamydia trachomatis; COVID-19; incidence; Denmark; disease surveillance.

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SIGNIFICANCE

Chlamydia trachomatis is a notifiable sexually transmitted infection of public health importance. It was suggested that, during the COVID-19 lockdown people would be discouraged from seeking medical attention. This study shows that this was true for the first strict lockdown, but that normal screening returned quite quickly once restrictions were eased, and that, overall, since the beginning of the pandemic *C. trachomatis* cases have remained at an expected level compared with data for 2018 to 2019.

COVID-19 was declared a pandemic on 11 March 2020 (1). In Denmark, a strict lockdown was implemented which restricted workplace and school attendance, while encouraging residents to stay home (2). COVID-19 restrictions have remained in place, with varying stringency to 1 February 2022. These restrictions have had a plethora of behavioural and psycho-social effects (3).

Danish COVID-19 restrictions have, as expected, been associated with notable reductions in the incidence of infectious diseases, such as influenza, and pertussis, as well as invasive meningococcal and pneumococcal infections (4, 5). Perhaps less expected, COVID-19 restrictions have also been associated with a dramatic reduction in extremely preterm birth (6, 7). This raises the question, could a reduction in infectious disease burden, particularly ascending urogenital infections (UGIs), several of which have been associated with preterm birth (8), explain the reduction in extremely preterm birth? While we cannot answer this question directly, we can assess the incidence of chlamydia within the Danish population as a proxy for transmissible UGIs.

In Denmark, chlamydia is the most frequent bacterial sexually transmitted infection (STI), and it has been subject to mandatory laboratory notification since 1994. In addition, *Chlamydia trachomatis* infection either co-occurs or shares predisposing risk factors with several UGIs, e.g. bacterial vaginosis (9) or genital mycoplasmas (10), which makes it a possible surrogate marker for a broader range of, non-notifiable, UGIs.

We hypothesized that the incidence of *C. trachomatis* infections would reflect behavioural changes induced by the COVID-19 restrictions in Denmark. Using publicly available data originating from The Danish Microbiology Database (MiBa) (11) via the webportal at Statens Serum Institut (12), alongside national surveillance data pertaining to the number of tests performed (13), we compared the incidence of laboratory-verified *C. trachomatis* infections since the initiation of COVID-19 restrictions with that of the preceding 2 years, 2018 to 2019. The incidences were contextualized using lockdown stringency

information from the Oxford COVID-19 Government Response Tracker (OxCGRT) (14, 15) and mobility data from Google COVID-19 Community Mobility Reports (16).

METHODS

Data sources

Numbers of laboratory-confirmed *C. trachomatis* infections were obtained via extracts from MiBa via the webportal at Statens Serum Institut (11, 12). The monthly number of *C. trachomatis* laboratory tests performed since January 2018 was obtained from national surveillance data extracted from MiBa (13). Lockdown stringency data were obtained from OxCGRT (14, 15). Mobile phone-based location data were obtained from Google COVID-19 Community Mobility Reports (16). With the exception of the national surveillance data (13), all data were obtained from publicly available sources.

Study periods

This study examined the period since the first containment policies were enacted following the report of the first Danish COVID-19 cases on 27 February 2020 until 31 March 2021 (**Fig. 1**). The first-wave lockdown (12 March to 14 April 2020), was followed by a period in which restrictions were eased, only to be tightened again with increasing infection rate, in the second-wave lockdown (17 December – 31 March 2021) (Fig. 1). The period of COVID-19 restrictions was compared with the aggregate data from the same

calendar periods for the years 2018 to 2019. Sex and age distributions were compared with data from 2015 to 2019.

Statistical analysis

We describe here incidence rates (number of laboratory-confirmed *C. trachomatis* infections / population at risk on 1 January of the relevant year) according to age, sex, period, and geographical region (province of residence). The number of tests performed is described per month since January 2018. The study compares the number of tests performed using Poisson regression, offset by population size to estimate rate ratios (RRs) with 95% confidence intervals (95% CIs). RRs were adjusted for period (2018 to 2019, 2020, and 2021). Odds ratios (ORs) with 95% CIs were estimated, comparing the odds of a positive test result (among all tests) according to period. Statistical analysis was conducted using R version 4.0.3.

Patient and public involvement

The research question was formulated as a response to public interest expressed through media contacts. No patients were involved, as the study was an anonymous register study. The results are disseminated both via scientific journals and media reports.

Ethics

All data were aggregate and most from publicly available sources supplemented with national surveillance data, hence no approval from scientific ethics committees or data authorities were necessary, as per Danish law and regulations.
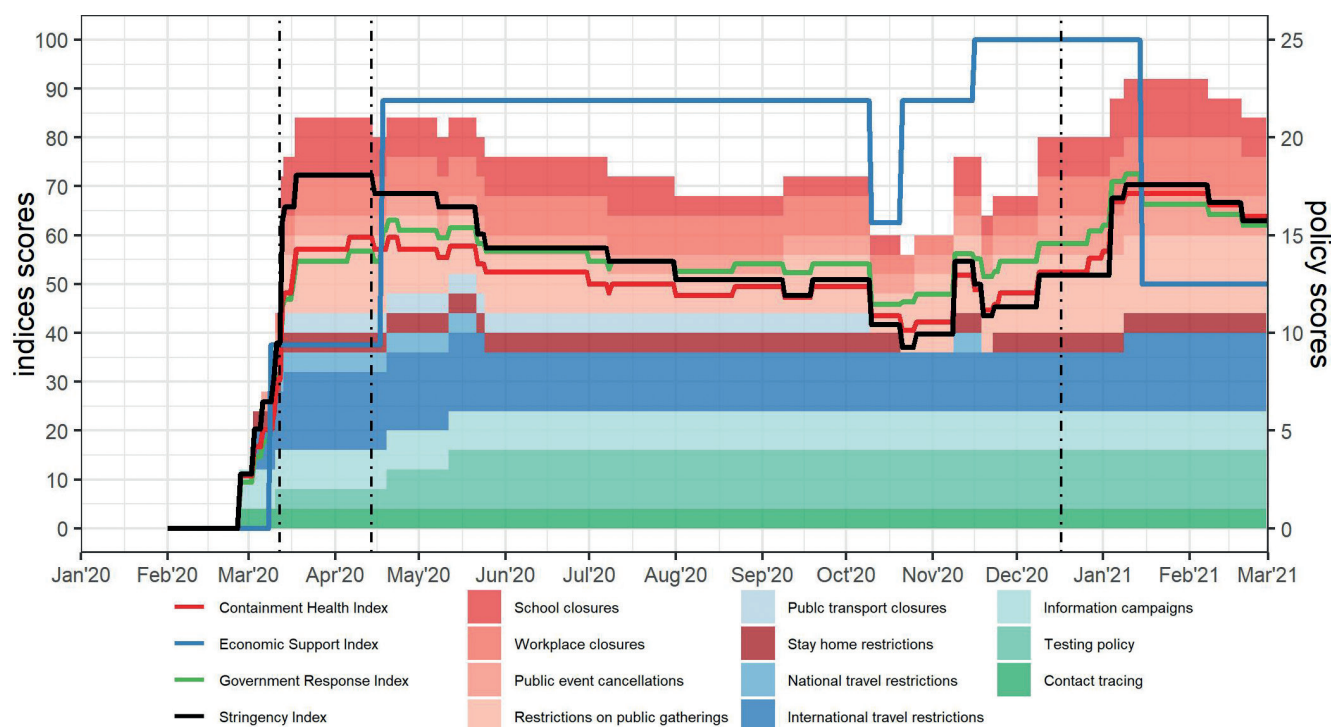

Fig. 1. Danish COVID-19 restrictions, the *black line* represents the overall stringency index, the *stacked coloured columns* represent the measures of the containment and control policies implemented during the whole COVID-19 restriction period. The lockdown periods are indicated between the vertical dot-dashed lines, the first lockdown occurred between 12 March – 14 April, 2020 and the second lockdown occurred between 17 December – 31 March, 2021. The coloured lines represent containment, economic support, and government response indices, respectively. Data source for panel B: https://www.bsg.ox.ac.uk/research/research-projects/covid-19-government-response-tracker#data (14). The *black dot-dashed vertical* lines define the extent of the 2 strict lockdown periods.

Table I. Incidence rates per COVID-19 restriction period compared with the same periods in 2018 to 2019

Period	Pre-COVID-19 restrictions Crude IR	COVID-19 restrictions Crude IR	Tests performed aRR	2.5% CI	Test positivity 97.5% CI	OR	2.5% CI	97.5% CI
March–April	88.3	66.5	0.72	0.71	0.73	0.98	0.96	1.00
May–December	96.6	99.8	0.96	0.96	0.97	1.03	1.02	1.04
January–March	93.7	95.9	1.01	1.01	1.02	0.98	0.97	0.99
Total	96.1	93.8	0.93	0.92	0.93	1.06	1.04	1.07

Mean test positivity values were calculated from January 2018 to February 2020.
aRR: adjusted rate ratio; CI: confidence interval; IR: incidence rate, per 100,000 population.

RESULTS

The crude incidence rate (IR) of laboratory-confirmed chlamydia infection was 66.5 per 100,000 population during the first lockdown March–April 2020, compared with a crude IR of 88.3 per 100,000 population in March–April 2018 to 2019 (**Table I**). However, the adjusted rate ratio (aRR) of tests performed in both periods was 0.72 (95% CI 0.71–0.73), whereas the OR of having a positive test was 0.98 (95% CI 0.96–1.00) (Table I). This, and the monthly number of tests performed (Table SI), suggests that the reduced crude IR in the first lockdown period is caused by reduced testing. During the May to December 2020 restriction period and the second lockdown, in January 2020 to March 2021, the crude IRs of laboratory-confirmed chlamydia infection were similar to the crude IRs of the same periods in 2018 to 2019 (Table I). In the same periods the overall aRR of tests performed and the test positivity were similar to the values noted for 2018 to 2019 (Table I and Table SI).

The Danish COVID-19 policies are shown in Fig. 1. The first Danish COVID-19 case was found on 27 February 2020, and this was followed by information campaigns, introduction of testing and contact tracing, travel restrictions, and other containment strategies (17) (Fig. 1). On 12 March 2020, when the number of COVID-19 cases rose dramatically and the WHO declared COVID-19 a pandemic, strict lockdown measures were introduced, with workplace and school closures, as well as stay home restrictions. This lockdown period lasted until 14 April 2020, when a gradual easing commenced. This period of lessened COVID-19 restrictions, lasted until late December 2020, where the second wave of the pandemic necessitated a second lockdown that was still in effect at the end of March 2021.

The mobility information from Google (Fig. S1) demonstrates the behavioural consequences of the lockdown period, with a reduction (~60%) in workplace presence and an increase (~18%) in the proportion of time spent in places of residence during the first lockdown period. The second lockdown did not result in an effect similar to the first, as a reduction of only ~30% (except for a short reduction to ~60% during Christmas holidays) in workplace presence, and an increase of ~12% of time spend in places of residence during the second lockdown period were noted (Fig. S1). This behavioural difference was seen despite a similar level of formal lockdown stringency (Fig. 1). Thus, the first lockdown period was associated with a reduction in testing for *C. trachomatis* as well as a reduction in laboratory-confirmed chlamydia infections, followed by a relative increase in testing and number of infections between May and December 2020, whereas the second lockdown period was characterized by a marginal increase in the number of tests performed, and a marginal reduction in test positivity (Table I, Table SI).

The monthly chlamydia incidence in women and men (Fig. S2) distributed in age groups, demonstrates a reduction in laboratory-confirmed cases during the first lockdown and an increase in July 2020 (Table SI). No significant deviation from the numbers for 2015 to 2019 was seen in either sex or age-groups during the second lockdown from January 2020 to March 2021.

The chlamydia incidence in the 11 provinces of Denmark is shown in Fig. S3. No marked differences in temporal development between provinces were observed, suggesting that the behaviour changes associated with COVID-19 restrictions were uniformly spread throughout Denmark.

The ratio between the number of men and women with chlamydia was < 0.6 in persons aged 15–24 years, but increased with age (Fig. S4) to > 1 in persons aged 45–54 years. This picture is compatible with the pre-COVID lockdown epidemiology of chlamydia (18). However, a decrease in the ratio in March, followed by an increase in April and May 2020, in persons in the age group 45–54 years was noted.

DISCUSSION

The first lockdown period was associated with a moderate, ~25%, decrease in laboratory-confirmed cases of *C. trachomatis* (Table I). However, this period was also associated with a similar decrease in laboratory tests performed (Table I) and accounting for that showed that in fact there was no change in the odds of receiving a laboratory-confirmed chlamydia diagnosis during the first lockdown and the mean odds for the same period between 2018 and 2019 (Table I). This suggests that the decrease in IR is caused by reduced testing. The second lockdown showed a nominal increase in chlamydia cases (Table I) despite being formally as stringent as the

first lockdown (Fig. 1). However, the number of tests performed also increased marginally during the second lockdown and, after accounting for this, there is a small reduction between the odds of receiving a laboratory-confirmed chlamydia diagnosis during the second lockdown and the corresponding odds during the same period in 2018 to 2019. This suggests that the behavioural response was markedly more relaxed during the second lockdown than during the first lockdown (Fig. S1). The fact that the incubation time is 7–21 days for chlamydia indicates that the diagnostic effort subsequent to symptomatic disease could reflect sexual activity before lockdown. However, this effect will be much less for asymptomatic opportunistic screening cases.

The period between the first and second lockdowns was associated with a marginal increase in the IR of laboratory-confirmed chlamydia driven by an increase in test positivity between June and September, possibly explained by delayed testing. Indeed, in mid-March the Danish Organization of General Practitioners and the Danish Society of General Medicine issued a recommendation (19) that only patients with acute disease should attend GP surgeries, and consultations should preferentially be conducted over the phone. This may have resulted in some delay in testing, particularly as 70–80% of chlamydia infections in Denmark are asymptomatic, and most tests are performed as part of opportunistic screening. The restrictions for attending GP surgeries were lifted in April, 2020, making it worthwhile considering whether planned or delayed tests were simply performed over the following months. In addition, the statement that "Sex is good, sex is healthy, the Danish Health Authority is in favour of sex", purported broadly by the director of the Danish Health Authority in the Danish media in April 2020 (20) may have contributed to a normalization of sexual behaviours and consequent normalization of chlamydia cases. It cannot be excluded that the decrease in testing, and consequent decrease in incidence of laboratory-confirmed cases, seen in March–April 2020 was caused, at least in part, by reduced sexual activity among teenagers and young adults during the first lockdown; however, the period also saw a marked increase in online dating internationally (21) as well as in Denmark (22), suggesting that reduced sexual activity was not the explanation. The sex distribution of laboratory-verified cases of chlamydia during the COVID-19 restrictions was similar to that seen in the previous years, suggesting that the overall epidemiology was unchanged (Fig. S4). Likewise, the temporal variation in incidence of chlamydia during the COVID-19 restrictions was not influenced by sex (Fig. S2) nor by geographical location (Fig. S3).

Overall, the Danish COVID-19 restrictions, during the first lockdown, were associated with a decrease in the extent of testing and, consequently, of incidence of laboratory-confirmed chlamydia. The COVID-19 restrictions had very little, if any, effect on transmission of chlamydia in Denmark. Similar findings were reported from Finland, where *C. trachomatis* and *Neisseria gonorrhoeae* incidence were completely unperturbed during the first 5 months of the pandemic and lockdown measures (23). This is in contrast to cities in Italy and Spain, where the number of STIs (syphilis, gonorrhoea and chlamydia) dropped precipitously during the lockdown (24, 25). However, in Trento, Italy, the number of cases in 2020 was comparable to that in 2019, and risky sexual behaviour was not reduced (26). The difference between parts of Italy and Spain and northern Europe may be the extent to which tourism contributes to the incidence of STIs (24), as well as the extent to which the population follows the recommendations and instructions of the health authorities. In the USA, a slightly different pattern was seen, with a decrease in chlamydia of ~20% compared with 2019, and a smaller decrease in gonorrhoea and an unchanged incidence of syphilis (27). It is possible that the significant reductions in all STIs depend on whether a curfew is part of the lockdown restrictions. The lack of correlation between limitations in mobility and social interaction and chlamydia incidence may be a result of the extent to which dating apps were used, which are particularly important among young adults (21, 28),

In conclusion, the first Danish lockdown period was associated with a decrease in testing and a subsequent reduction in the incidence of laboratory-confirmed chlamydia. This was not seen in the second lockdown period and the intervening period of eased restrictions. Thus, the period of COVID-19 restrictions, with its significant effects on behaviour, was not associated with appreciable changes in chlamydia transmission.

ACKNOWLEDGEMENTS

REFERENCES

1. World Health Organization (WHO). WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. [accessed 2021 May 14]. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.
2. Klinker Stephensen E, Stærmose Hansen T. [Denmark is closing down: Here are the government's new initiatives]. [accessed 2021 May 17]. Available from https://nyheder.tv2.dk/samfund/2020-03-11-danmark-lukker-ned-her-er-regeringens-nye-tiltag.
3. Veer IM, Riepenhausen A, Zerban M, Wackerhagen C, Puhlmann LMC, Engen H, et al. Psycho-social factors associated with mental resilience in the Corona lockdown. Transl Psychiatry 2021; 11: 67.
4. Statens Serum Institut. Individually notified diseases 2020. [accessed 2021 May 21]. Available from https://en.ssi.dk/-/media/arkiv/uk/news/epi-news/2021/epi-news_11-17_2021.pdf?la=en.

5. Statens Serum Institut. The 2019/20 influenza season was very unusual. [accessed 2021 May 21]. Available from https://en.ssi.dk/news/news/2020/the-2019-20-influenza-season-was-very-unusual.

6. Hedermann G, Hedley PL, Baekvad-Hansen M, Hjalgrim H, Rostgaard K, Poorisrisak P, et al. Danish premature birth rates during the COVID-19 lockdown. Arch Dis Child Fetal Neonatal Ed 2021; 106: 93–95.

7. Hedley PL, Hedermann G, Hagen CM, Baekvad-Hansen M, Hjalgrim H, Rostgaard K, et al. Preterm birth, stillbirth and early neonatal mortality during the Danish COVID-19 lockdown. Eur J Pediatr 2022; 181: 1175–1184.

8. Force USPST, Owens DK, Davidson KW, Krist AH, Barry MJ, Cabana M, et al. Screening for bacterial vaginosis in pregnant persons to prevent preterm delivery: US Preventive Services Task Force recommendation statement. JAMA 2020; 323: 1286–1292.

9. Thorsen P, Vogel I, Molsted K, Jacobsson B, Arpi M, Moller BR, et al. Risk factors for bacterial vaginosis in pregnancy: a population-based study on Danish women. Acta Obstet Gynecol Scand 2006; 85: 906–911.

10. Ma C, Du J, Dou Y, Chen R, Li Y, Zhao L, et al. The Associations of Genital Mycoplasmas with Female Infertility and Adverse Pregnancy Outcomes: a Systematic Review and Meta-analysis. Reprod Sci 2021; 28: 3013–3031.

11. Voldstedlund M, Haarh M, Molbak K, MiBa Board of R. The Danish Microbiology Database (MiBa) 2010 to 2013. Euro Surveill 2014; 19: 20667.

12. Statens Serum Institut. [Monitoring in numbers, graphs and maps]. [accessed 2021 May 17]. Available from: https://statistik.ssi.dk/.

13. Schonning K, Dessau RB, Jensen TG, Thorsen NM, Wiuff C, Nielsen L, et al. Electronic reporting of diagnostic laboratory test results from all healthcare sectors is a cornerstone of national preparedness and control of COVID-19 in Denmark. APMIS 2021; 129: 438–451.

14. Blavatnik School of Government. COVID-19 government response tracker. [accessed 2021 May 17]. Available from: https://www.bsg.ox.ac.uk/research/research-projects/covid-19-government-response-tracker.

15. Hale T, Angrist N, Goldszmidt R, Kira B, Petherick A, Phillips T, et al. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). Nat Hum Behav 2021; 5: 529–538.

16. Google. Google COVID-19 Community Mobility Reports. [accessed 2021 Mar 4]. Available from: https://www.google.com/covid19/mobility/.

17. Danish Parliament. [The handling of covid-19 in the spring of 2020 – report submitted by the investigation group set up by the Danish Government's Committee on the Rules of Procedure regarding the handling of covid-19.]. Folketinget, 2021 (in Danish).

18. Gormsen AB, Diernaes JEF, Hoffmann S, Koppelhus U. [Chlamydia in Denmark]. Ugeskr Laeger 2018; 180: V01180040 (in Danish).

19. PLO, DSAM. [General practice during the corona epidemic – which patients can general practice fit and how?]. [accessed 2021 May 21]. Available from: https://www.laeger.dk/sites/default/files/almen_praksis_rolle_under_corona_plo_og_dsam15.3.20.pdf.

20. DR. [Brostrøm gives the green light to singles, sex is good sex is healthy.]. [Access 18/05/2021] Available from: https://www.dr.dk/nyheder/indland/brostrom-giver-gront-lys-til-singler-sex-er-godt-sex-er-sundt.

21. Tinder. Quarantine became the world's largest icebreaker on Tinder. Tinder Newsroom, 2020. [Accessed 18 May 2021] Available from: https://www.tinderpressroom.com/news?item=122476.

22. Terp S. [Online dating storms forward: "The last few months have been pretty severe"]. [accessed 2021 May 18]. Available from: https://www.berlingske.dk/virksomheder/onlinedating-stormer-frem-de-seneste-maaneder-har-vaeret-ret

23. Kuitunen I, Ponkilainen V. COVID-19-related nationwide lockdown did not reduce the reported diagnoses of Chlamydia trachomatis and Neisseria gonorhoeae in Finland. Sex Transm Infect 2021; 97: 550.

24. de Miguel Buckley R, Trigo E, de la Calle-Prieto F, Arsuaga M, Diaz-Menendez M. Social distancing to combat COVID-19 led to a marked decrease in food-borne infections and sexually transmitted diseases in Spain. J Travel Med 2020; 27: taaa134.

25. Sacchelli L, Viviani F, Orioni G, Rucci P, Rosa S, Lanzoni A, et al. Sexually transmitted infections during the COVID-19 outbreak: comparison of patients referring to the service of sexually transmitted diseases during the sanitary emergency with those referring during the common practice. J Eur Acad Dermatol Venereol 2020; 34: e553–e556.

26. Balestri R, Magnano M, Rizzoli L, Infusino SD, Urbani F, Rech G. STIs and the COVID-19 pandemic: the lockdown does not stop sexual infections. J Eur Acad Dermatol Venereol 2020; 34: e766–e768.

27. Crane MA, Popovic A, Stolbach AI, Ghanem KG. Reporting of sexually transmitted infections during the COVID-19 pandemic. Sex Transm Infect 2021; 97: 101–102.

28. Ansari A, Klinenberg E. Modern romance. New York: Penguin Press; 2015.