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journal homepage: www.elsevier.com/locate/lanwpcSpatiotemporal analysis of 11 years of *Chlamydia trachomatis* data from southern ChinaM. Kumi Smith^a, Kelly M. Searle^a, Wenyue Yang^b, Erica Rapheal^a, Cheng Wang^c, Peizhen Zhao^c, Ligang Yang^c, Shujie Huang^c, Bin Yang^{c,*}^a Division of Epidemiology & Community Health, University of Minnesota Twin Cities, 1300 South 2nd Street, Ste 300, Minneapolis, MN, USA^b College of Forestry and Landscape Architecture, South China Agricultural University, Guangzhou, China^c Dermatology Hospital of the Southern Medical University, No. 2 Lujing Road, Guangzhou, China

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ABSTRACT

Background: Urogenital *Chlamydia trachomatis* is the most prevalent bacterial sexually transmitted infection (STI) globally. Reviews suggest high and persistently endemic STI epidemics in low and middle income countries. However population-based prevalence estimates in these settings are less common, underscoring the need for analyses of available data to characterize patterns of disease burden. We identified spatio-temporal clusters and key behavioral, social, or environmental factors contribution to transmission in order to inform the prioritization and targeting of evidence based interventions.

Methods: Using 11 years of data (2006–2016) from the chlamydia case report system of Guangdong, China, we identified county level spatio-temporal hot and cold spots using the Getis-Ord G_i^* statistic and discrete Poisson models in SaTScan 9.6. We also estimated associations between observed distribution patterns and area-level demographic, social, and economic factors using quasi-Poisson regression models that controlled for annual counts of certified laboratories to account for fluctuations in location-specific detection capacity.

Findings: Cluster analysis indicates an expanding chlamydia epidemic in Guangdong, with cases clustered in regions of greatest economic activity. Greater male-to-female sex ratio (RR, 3.63; 95% CI, 1.41–9.45) and greater urbanicity (RR, 2.44; 95% CI, 1.98–2.99) were predictive of higher chlamydia case occurrence.

Interpretation: We found that chlamydia case occurrence in Guangdong province has been accelerating over the past 11 years and that its expansion is tied to indicators of social and economic development. These estimates not only identify high prevalence regions to target but also areas where data gaps potentially remain. The salience of sex ratios and urbanicity may best be understood through the lens of China's modern history of labor migration which has reshaped the gender dynamics and health access landscape of urban China. Future chlamydia control efforts will require a population-based approach focused on reengaging sexually active adults of diverse economic and migratory backgrounds.

Funding: This was an unfunded study using routinely collected public health data.

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Research in context

Evidence before this study

We searched PubMed for studies published in English or Chinese up to November 9, 2020, using the search terms: (“chlamydia” OR “chlamydia trachomatis” OR “sexually transmitted diseases” or “sexually transmitted infection”) AND (“prevalence” OR “seroprevalence” OR “estimate” OR “geospatial” OR “spatial”) AND (“population-based” OR “general population” OR “”) AND (“China”). Article relevance was based on title and abstract review and were restricted to those conducted in mainland China and to populations other than those typically considered key populations such as men who have sex with men, female sex workers, or patients recruited at reproductive or sexual health clinics. References cited in the most relevant articles were also reviewed.

To our knowledge no other spatial or spatiotemporal analyses of chlamydia in China has yet been published in the peer-reviewed literature, though spatial analyses of gonorrhoea and syphilis in this setting are plentiful. However we did identify four publications estimating chlamydia prevalence in non-key populations using probability sampling methods to construct representative samples. Two were conducted using data from 1999–2000 and the other two from more recent data (2016 and 2018–2019). Other reports on chlamydia prevalence in non-key populations include estimations in samples of pregnant women, women seeking routine physical exams, or “normal population” members whose sera had been retained for an immunological analysis. All but one of the reports used nucleic acid amplification testing methods. Estimated prevalence rates for women ranged from 2.3% to 11.1% for women, though among population representative samples rates the range was much narrower (2.3% to 4.12%). Estimates for men ranges from 2.07% to 7.3%, though again, the upper range was much lower when restricted to population representative sample (2.7%).

Added value of this study

Our study assessed clusters of reported chlamydia in a historically high prevalence region of southern China where rapid social and economic development has shaped the sexual health landscape. Our analysis was conducted at the county level and assessed for both hot and cold spots. We also analyzed the association of hot spots with economic development indicators including GDP per capita and GDP growth, as well as social development indicators including sex ratios and urbanicity. Our models improved on past geospatial analyses of case report data by adjusting for the annual cumulative numbers of certified laboratories in each region, in order to control for varying reporting capacity of each region. Clustering in our data was also assessed using three different statistical approaches and hot/cold spot analysis was assessed using two methods.

Implications of all the available evidence

To our knowledge this is the first in-depth spatiotemporal analysis of chlamydia infection in any part of China, and one of few descriptive analyses of its distributions or patterns in the past 20 years. Though case report data for highly asymptomatic infections such as chlamydia are known to underestimate true disease burden, their patterns and distributions over time can identify groups or regions to prioritize for interventions or places where data collection must be strengthened. The increasing trend of reported chlamydia, particularly in recent years when the data reporting system has already matured, suggest an ongoing expansion of this epidemic. The salience of the male-to-female sex ratio and urbanicity in

predicting chlamydia occurrence are notable and may indicate a considerable burden of disease in regions where migrant laborers make up a significant portion of the local population. The lack of sexual health education in China for populations not considered to be at high risk of HIV infection and relatively poorer health access among migrants are two key starting points for addressing the increasing burden of chlamydia in sexually active adults.

1. Introduction

Urogenital *Chlamydia trachomatis* is the most prevalent bacterial sexually transmitted infection (STI) globally, with an estimated 131 million new case occurring each year [1]. Untreated chlamydia infection can lead to serious complications such as female infertility or ectopic pregnancy and may also increase risk of HIV transmission and acquisition [2]. The global burden of chlamydia-associated pelvic inflammatory disease, infertility, and ectopic pregnancy are not well defined, especially in low- and middle-income countries (LMIC) where STI surveillance systems are incomplete or under resourced [3]. However given what is known about its disproportionate impact on young adults of reproductive age and prevalence in infertility clinic patients, chlamydia morbidity burden is thought to be sizeable [4]. Where available, data suggests that rates of curable STIs in many LMIC are high and persistently endemic [5], likely due both to evolving sexual lifestyles under rapid urbanization as well as uneven availability of prevention services such as sexual education or routine STI testing [6]. The infrequency of noticeable symptoms means chlamydia infection commonly goes unrecognized by the infected person, underscoring the importance of screening programs for effective control. A better understanding of where and how cases occur is essential for informing the design and targeting of effective programs.

China's current STI epidemic is growing increasingly severe. After their near elimination under the strict social control measures of China's socialist regime in the 1950s, bacterial STIs have resurged since the economic opening up of the early 1980's [7]. Most epidemiological studies of chlamydia in China to date have focused on key populations such as patients of sexual or reproductive health clinics [8], female sex workers and their clients [9,10], or men who have sex with men (MSM) [11], leaving a dearth of understanding about its burden or distribution in the population at large. To impact population level disease burden, however, insights into its distribution transmission patterns in the entire population are needed. Only two population-based studies of chlamydia have been conducted in China since 2000 [12,13]. Both reports suggest the presence of an expanding chlamydia epidemic, but as cross sectional studies they lack the ability to explore larger societal or temporal factors that may be driving its spread. In settings like China with sufficiently developed primary healthcare systems and disease reporting infrastructure, descriptive analyses of reported case data can provide insights on key drivers and generate novel hypotheses. Spatial analyses of other STI case report data in China have already contributed important scientific knowledge to inform disease control measures. However these reports do not analytically distinguish between possible changes in the force of infection and evolving capacity of surveillance systems to detect and report cases [14,15]. Nor have any to date been conducted on chlamydia, by far the most prevalent curable STI.

We analyzed spatio-temporal patterns of chlamydia cases in Guangdong province, a high transmission region of southern China, using 11 years of data (2006–2016) from the provincial case report system. We estimate associations between spatio-temporal

case clusters and key behavioral, social, or environmental factors to inform the prioritization and targeting of evidence based interventions. The fast yet uneven economic development of southern China since the 1980's also make lessons from Guangdong particularly instructive for other low and middle income settings undergoing similarly rapid social and economic change. By considering not only case trends but also the evolving nature of the reporting systems themselves, this analysis seeks to provide a more objective investigation into threats and opportunities for chlamydia control.

2. Methods

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for the reporting of observational studies [16].

2.1. Guangdong province

Guangdong province has been a global center of trade since pre-modern times, in particular the central cluster of nine cities that make up the Pearl River Delta region. Its regional STI epidemic was well documented by local and foreign authorities by the 20th century, who attributed it to widespread prostitution and economic disparity [17]. Following the decades-long STI suppression campaign from the 1950's to 1970's under Maoist health policies, chlamydia, like other STIs, has made a massive resurgence since the economic re-opening of the 1980's, a phenomenon that has been attributed, among other things, to social change, population mobility, and rising costs of healthcare [17,18], in which nearly the entire population was rendered susceptible through curative treatments [17]. Guangdong's prominence as the modern day chlamydia epicenter may also be partially due to its highly developed STI case reporting system which has been collecting chlamydia case reports since 2006.

2.2. Data sources

Information about confirmed cases of CT were retrieved from the provincial case-based surveillance system maintained by the Dermatology Hospital of the Southern Medical University in the provincial capital of Guangzhou. Chlamydia has been a reportable disease in Guangdong province since 1985, and a web-based case report system was established in 2006. Confirmed cases were those who, regardless of symptoms, had at least one laboratory confirmed test result, whether by means of microscopy, culture, antigen testing, or by nucleic acid amplification testing (NAAT). In addition to geocodes for patient residence and the of diagnosis, case reports also provide information on each case's gender, age, occupation, and a host of other variables; however due to substantial missingness (68–76%), only age, gender, and occupation was retained. Occupations were classified as follows: lower skilled jobs included those involving manual labor such as day laborer, farmer, fisherman, or housekeeper whereas higher skilled jobs included occupations such as teachers, office workers, government workers, students, or business owners. Only cases over the age of 15 were retained for the analysis. Because of the division or consolidation of counties over time, county geocodes were revised from those included with the shape file to match the list of counties in the case reporting dataset.

Regarding area-level variables, the annual number of certified laboratories operating in each city was provided by the Dermatology Hospital of the Southern Medical University. Data on county level population, gross domestic product (GDP) per capita, and GDP growth rate were obtained from the 2015 provincial census data available from the Guangdong Statistical Yearbook of 2015 from the

Guangdong Province Statistical Information Net. Data on urbanicity was obtained from the Land cover/Land use from the Global Land Cover 2000 project developed by the European Commission's Science and Knowledge Service Joint Research Center [19]. Land cover data was converted into an urbanicity index by classifying all land cover categories described as "cultivated," "managed," or "urbanized" as urban and the remainder (described as "non-managed" or "non-urban") as rural. Joining the land use raster file to the polygon shape file then allowed us to calculate the urbanicity index, or the proportion of each county whose land area was classified as urban.

2.3. Statistical analysis

Clustering of cases was assessed using three approaches. Global Moran's I values were calculated to assess spatial autocorrelation (overall clustering) in cases of chlamydia reported in 2016 only. Moran's I values range from negative one (dissimilar values cluster together) to one (similar values cluster together), with zero representing random spatial distribution. Correlograms were then used to plot lagged orders of smoothed of the Moran's I using a binary scheme that indicates whether a county shares a boundary with another county or not. Separate correlograms were used to compare lagged orders for observed rates versus spatially smoothed ones which used a weight matrix that replaces each county count with the average of its rate and its neighboring rates. Spatio-temporal clustering was then assessed using all years of data (2006–2016). First, a hot and coldspot analysis was conducted in ArcGIS 10.6.1 in which the Getis-Ord G_i^* statistical method was derived to identify counties where observed cases counts are significantly higher or lower than expected if cases occurred completely at random. Discrete Poisson models in SaTScan 9.6 were then used as a second method of identifying clusters. The model consists of a space-time scan statistic that uses a cylindrical scanning window in which the circular base corresponds to spatial clustering and its height to temporal clustering in order to identify points in space and time when case counts exceeded or were less than occurrences expected if were cases randomly distributed. The model specified a maximum circular spatial cluster size of 40% of the population and a maximum temporal period of 30% of the study period, and no cluster centers were permitted to be in other clusters.

To identify variables associated with spatial variation in area-level outcomes, we used quasi-Poisson regression models with case counts per population as the outcome and the total population as the offset to account for over-dispersion. We also adjusted for study year and the number of certified laboratories operating in each city to control for effects of location-specific detection and reporting capacity.

IRB approval was obtained from Dermatology Hospital of the Southern Medical University to conduct this analysis. Data used in this analysis were collected for routine public health surveillance and were deidentified. Data are from the Guangdong provincial case report system and are property of provincial Center for STD Control & Prevention. It is collected for disease control purposes and can only be used for epidemiological research on a case by case basis determined by the IRB of the Dermatology Hospital of the Southern Medical University.

3. Role of funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Table 1
Characteristics of the 419,627 cases reported over the 11 years of the study period.

	Male cases N (%)	Female cases N (%)
Total	112648	270043
Age		
25 and under	20351 (18.07)	90045 (33.34)
Over 25	92297 (81.93)	179998 (66.66)
Reporting clinic		
Comprehensive hospital*	84669 (75.16)	171566 (63.53)
MCH, OBGYN	5926 (5.26)	65372 (24.21)
STI, GUM	3353 (2.98)	1828 (0.68)
Other	13344 (11.85)	23621 (8.75)
Missing	5356 (4.75)	7656 (2.84)
Occupations**		
Lower skilled	62041 (55.08)	175479 (64.98)
Higher skilled	34420 (30.56)	56743 (21.01)
Unknown or missing	16187 (14.37)	37821 (14.01)
Rurality		
Lives in ≥ 50% rural county	34562 (30.68)	94673 (35.06)
Lives in < 50% rural county	79212 (70.32)	193891 (71.8)
Traveled outside of home or adjacent county for diagnosis		
Yes	6986 (6.2)	21853 (8.09)
No	105662 (93.8)	248190 (91.91)

MCH: maternal and child health
 OBGYN: obstetrics and gynecology
 STD: sexually transmitted infection
 GUM: genitourinary medicine

* Includes western, traditional Chinese, and integrated
 ** Lower skilled jobs included those involving manual labor such as day laborer, farmer, fisherman, or housekeeper. Higher skilled jobs included occupations such as teachers, office workers, government workers, students, or business owners.

4. Results

A total of 402,338 reported cases of confirmed chlamydia were included in the final analysis (Table 1) after removing 330 cases under the age of 15 (0.08%), another 848 whose listed residence was outside of Guangdong province (0.2%) and another 17,289 cases whose residential geocodes could not be identified in the list of geocodes in the shape file (4.1%). Female cases made up the vast majority of the sample (71.1%), who were on the whole younger than their male counterparts (33.1% versus 18.0% of cases were under the age of 25). Most cases were diagnosed and reported by comprehensive hospitals (also known as “general hospitals” which admit all types of medical and surgical cases; 66.6%), though a notable share of female cases were also diagnosed in maternal child health centers (24.4% versus 5.7% for men; men are usually diagnosed in MCH centers as part of partner referral programs). In terms of reported occupation, female cases were more likely to report lower skill jobs such as farming or domestic work as opposed to higher skilled jobs such as retail or government jobs. About a third of all cases lived in more urban counties—that is, where more than half the land is developed for non-agricultural purposes (30.7% for male; 35.1% for female). Nearly all cases regardless of sex were diagnosed in the same or neighboring county, though a slightly higher portion of female cases traveled beyond for care compared to their male counterparts (8.09% versus 6.2%).

Plots of case counts per 10,000 over time indicate a consistent rise in cases over time. Both male and female incidence undergo a notable jump after the first two years during initial implementation of the reporting system. By the end of the observation period reported incidence for men and women had reached 2.8 per 10,000 for men and 10.2 per 10,000 for women. Incidence was higher not only in women relative to men (Fig. 1, Panel A) but also in cities in the Pearl River Delta region relative to the rest of the province, most notably in Shenzhen (Fig. 1, Panel B).

Table 2
Quasi-Poisson regression model results. Each model adjusts for time and spatial effects, as well as for the time-varying number of labs in each city.

County-level variables	RR (95% CI)
M:F sex ratio of the county in 2010	3.64 (1.41–9.45)
Proportion of cases that are male (%)	0.80 (0.53–1.21)
Proportion of cases under 25 (%)	0.40 (0.20–0.77)
Proportion of cases that traveled for care (%)	0.19 (0.16–0.22)
GDP per capita (2015)	1.00 (1.00–1.00)
GDP growth (2015)	0.77 (0.74–0.79)
Urbanicity (%)	2.44 (1.98–2.99)

Spatial distribution of the cumulative number of cases throughout the entire observation period—2006 to 2016—are shown in Fig. 2. The choropleth in Panel A indicates spatial case distributions in which caseloads appear highest in the Pearl River Delta, the most populated and economically developed region of Guangdong province (outline in white on the choropleth on the map). Geographic distributions of other key area-level variables further show that the Pearl River Delta region is also has the highest concentration of urban land use, male -to-female sex ratios, and authorized medical laboratories (data is aggregated at the city level). However in terms of male -to-female sex ratios, coastal counties generally appear to have higher ratios relative to their inland counterparts. Regional distribution of laboratories (shown in Fig. 2, Panel D using data collected at the city level) shows that development of laboratory resources has lagged in the eastern and western-most regions.

Clustering of cases was apparent across the three methods of assessment. Plots of Global Moran’s I statistics over lagged spatial orders of neighbors—administrative units sharing a border—were used to examine the degree of autocorrelation as a function of distance. The statistic ranges from a value of 1 representing perfect autocorrelation to -1 representing perfect dispersion (0 represents no autocorrelation or perfect randomness). Plots in Fig. 3 indicate evidence of geospatial autocorrelation up to four orders (i.e. up to distances corresponding to four neighboring counties apart) for both direct and smoothed case rates, beyond which negative autocorrelation was evident only in the directly observed rates. The Getis-Ord G_i^* statistical method in ArcGIS (Fig. 4, Panel A) identified 25 counties with statistically significant z-score values greater than one ($p < 0.05$), indicating that case counts were higher than expected than had cases occurred at random (dark red counties in Fig. 3, Panel A). Eleven counties had statistically significant z-score values less than one ($p < 0.05$) and appeared in two separate clusters located on the eastern-most and western-most coastal regions of the province (dark blue counties in Figure 4, Panel A). Results of the SaTScan cluster analysis identified four hotspots and two cold spots. The relative chlamydia rates inside the two highest risk hot spot clusters (outlined in dark red in Fig. 4, Panel B), were 2.02 and 2.39 times the rate in the rest of the province, respectively. The two lowest risk cold spot clusters (in blue in the same figure) had 0.17 and 0.18 times that of the other clusters. Similar to the cluster detection results using the Getis-Ord G_i^* approach, case occurrence was higher than expected in the Pearl River Delta region, while fewer than expected cases occurred in the eastern- and western-most regions of the province.

Area-level variables predictive of higher count occurrence are reported in Table 2 and included higher male-to-female sex ratio (RR, 3.63; 95% CI, 1.41–9.45) and greater urbanicity (RR, 2.44; 95% CI, 1.98–2.99). Conversely the share of cases that were under 25, that had traveled for care, or who were male were inversely associated with a county’s case counts, though the last association lacked statistical significance (RR, 0.40; 95% CI, 0.20–0.77; RR, 0.19; 95% CI, 0.16–0.22; RR, 0.80; 95% CI, 0.53–1.21, respectively). GDP growth in 2015 was also inversely related to case occurrence (RR,

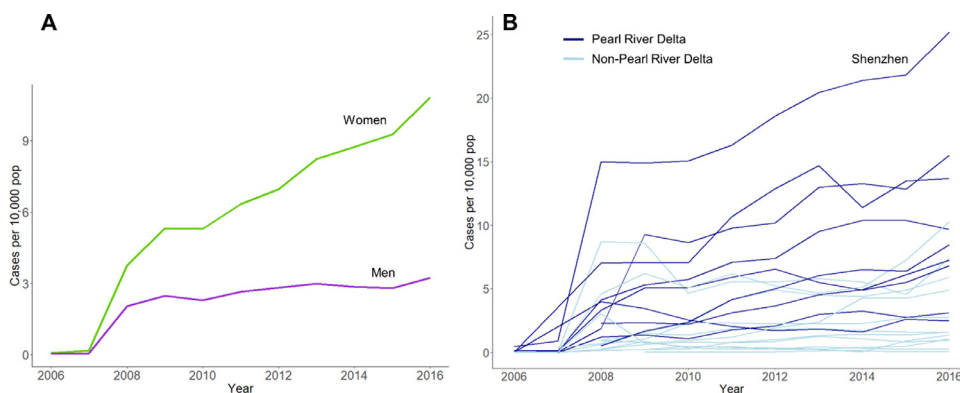


Fig. 1. Incidence of reported cases by gender and by city from 2006 to 2016.

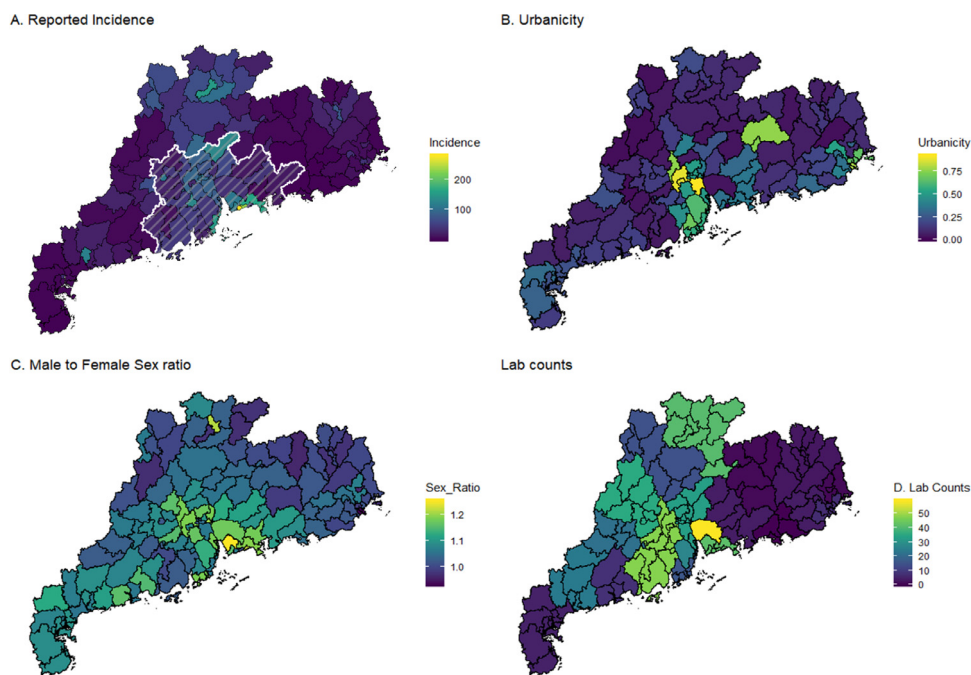


Fig. 2. Spatial distribution at the county level of A) Reported chlamydia per 10,000 population in most recent year of data (2016), B) urbanicity, C) male-to-female sex ratio, and D) numbers of labs.

0.77; 95% CI, 0.74–0.79), whereas GDP per capita in the same year had a null association (RR, 1.00; 95% CI, 1.00–1.00).

5. Discussion

Spatial-temporal patterns derived from 11 years of reported chlamydia cases in Guangdong province describe an expanding epidemic with cases clustered in regions of greatest economic activity. The incidence of reported chlamydia cases increased dramatically from the beginning to the end of the observation period, from 0.03 to 2.8 male cases per 10,000 and from 0.07 to 10.2 female case per 10,000. Based on the four known population-based estimates of chlamydia prevalence in China, true prevalence in women likely ranges from 0.9% to 2.6% and from 2.1% to 2.7% in men [7,12,13,20]. If we were to convert the most recent year (2016) of reported incidence from the case-based surveillance system into a population prevalence estimate using the commonly assumed average duration of disease of one year, the expected prevalence would be 0.1% in women and 0.03% in men. Nevertheless the long-standing nature of Guangdong’s STI case report system (first established in 1985) and the lack of explicit clinical screening guidelines or testing campaigns during the observation period

suggest that the sizeable increases in caseload is at least partially driven by elevated transmission.

Though a known feature of case-based surveillance data, this vast underestimation of true prevalence by surveillance data can also provide insights salient to design of effective control programs. First, a key driver of case under-ascertainment is the low pathogenicity of chlamydia infection; that is, the asymptomatic nature of most infections dampens care seeking and therefore timely case detection. Chlamydia control strategies in higher income settings have therefore commonly recommended routine screening for sexually active adults, mostly in women [21]. But such recommendations offer little guidance on ways to engage the vast numbers of sexually active adults who have no meaningful engagement with the healthcare system. The challenge is even greater in many LMIC where most sexual health promotion takes place in the context of HIV prevention and rarely engages groups who do not bear the label of an HIV “key population” (e.g. MSM, female sex workers). Catching up to the rapidly evolving sexual landscape of urban China therefore requires broader implementation of population-based screening for curable STIs and sexual health campaigns that can reach all sexually active people. A second insight offered by

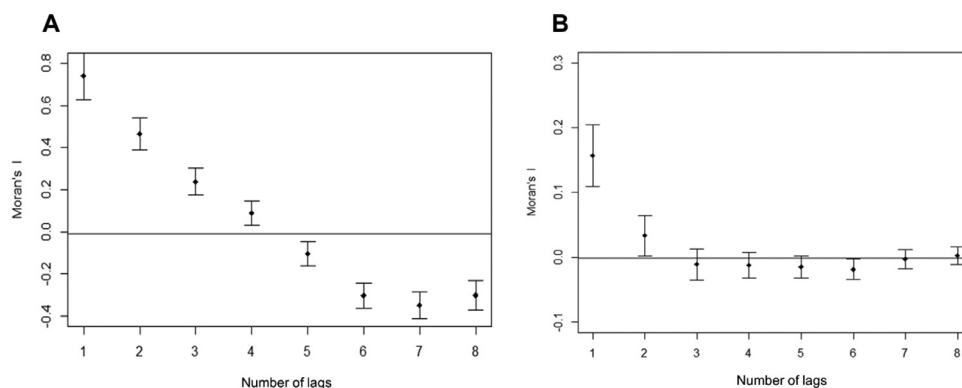


Fig. 3. Plots of Global Moran's I of reported chlamydia in 2016 (per 10,000 persons) for multiple order of neighborhood structures using directly observed case rates (Panel A) and using spatially smoothed rates (Panel B).

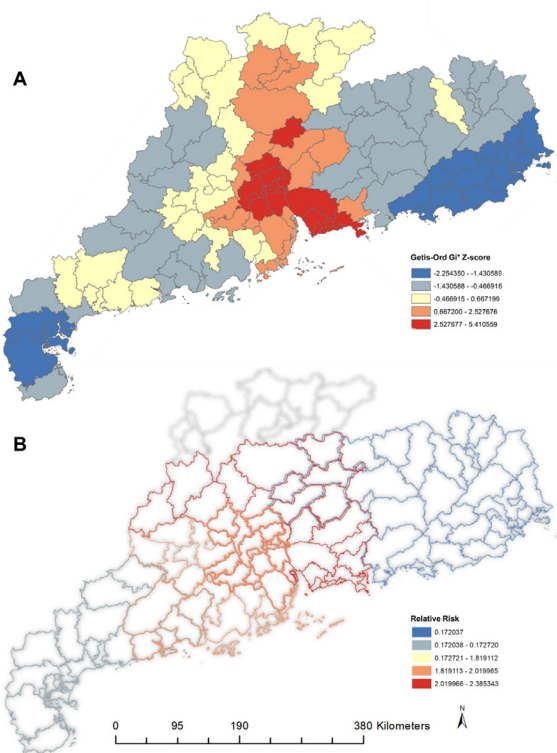


Fig. 4. Spatio-temporal cluster analysis using data from 2006 to 2016. Panel A shows counties identified using the Getis-Ord G_i^* statistical approach in ArcGIS as having more cases than expected in warmer hues and fewer cases than expected in cooler hues. Panel B shows clusters identified using SaTScan.

the case-based surveillance data is in the vast underrepresentation of male infections captured by the system. Asymptomatic cases in men account for a substantial reservoir of untreated infection that helps sustain transmission; given the dearth of official guidance on male-targeted strategies, design of population-based screening programs must consider ways to address the enduring challenge of male engagement in healthcare [21]. Beyond sex-specific service targeting, effective STI screening programs will also need to consider common barriers to sexual healthcare including lack of reliable information about STI prevention, the STI-related stigma and inadequate healthcare coverage in socioeconomically disadvantaged groups. Ongoing STI surveillance, particularly that which captures geocode data, will also be critical for designing and evaluating effective control programs by informing temporal and geographic distribution of cases.

The tendency for STI rates to concentrate geographically and its association with social and neighborhood factors has long been established [22]. Yet particular to our findings is the salience of the male-to-female sex ratio and urbanicity in predicting chlamydia occurrence, results that may best be understood through the lens of China's labor migrant experience. Though our case-based data does not include migrant status, we note the relatively high male-to-female sex ratios in the Pearl River Delta and southwestern coastal regions which are known as national migration destinations and where chlamydia prevalence is higher. China's intra-provincial migrant worker population is still largely male—64.9% in 2019—and given that nearly three quarters of the Pearl River Delta population is made of migrants, their gender makeup can significantly alter local demographics [23]. Higher ratios of men to women in China have been cited as a potential driver of STI transmission, not only due to the “surplus men” phenomenon but the pressures it generates for migrant women to participate in commercial or “survival” sex [24]. Others have also noted the relatively high prevalence of MSM who make up the population of rural-to-urban migrant men [25], possibly because this population is drawn by more sexually liberal urban culture. The extent to which the high chlamydia prevalence documented in this population [26] may be contributing to the clusters observed in our findings will require improved documentation of sexual behaviors in the case report system. Theories about the potential for MSM to act as a “bridge” for STI transmission to their female partners is largely based on prevalence of bisexual behaviors reported by this group; however little is yet known about the health status of the female partners themselves. The association of case rates with urbanicity also attests to the rigidity of the national household registration system which restricts access to public benefits once a person leaves their registered home county, a system that directly impacts migrant access to affordable healthcare and other resources [27]. In a departure from past findings about economic development and STIs in China and elsewhere [14,15] chlamydia case occurrence in our data was unassociated and even negatively associated with measures related to GDP. The story of STI resurgence in China—particularly in Guangdong—has always been framed as a byproduct of rapid economic development in the 1980's and 90's [17]. While a probable explanation for rapid STI spread in this initial phase of the country's economic and social reopening, a more uneven picture of economic prosperity has since emerged with growing income gaps and greater marginalization of those who have been left behind by the country's rapid development. Indeed, one more recent study did find that syphilis occurred in both high and low income counties [28]. Furthermore as a summary measure of economic productivity, GDP has been critiqued for its failure to account for factors more salient to human welfare such as equitable income distribu-

tion or economic well-being. Given the known link between socioeconomic status and sexual health in other settings [14,15], future research on China's STI epidemic may do well to consider exploring how GDP alternatives such as the Social Progress Index or the United Nations Development Fund's Global Multidimensional Poverty Index impact STI occurrence [29,30].

Findings from this study, as with all analyses of case-based surveillance data, should be considered in light of key limitations. Correct case ascertainment is heavily reliant on choice of diagnostic test and the reliability of complete case reporting. Unfortunately information about the specific laboratory test used is not a routine part of case reports. According to a 2020 survey of 651 hospitals in Guangdong, 16% of reporting entities reported using the immunochromatographic (ICT) assays for chlamydia detection, with the remainder using the officially recommended nucleic acid amplification test (NAAT). ICT has been shown to have high specificity but sensitivities can be as low as 30% with lower concentrations of *C. trachomatis* [31]. Test choice at each entity is largely determined by fiscal capacity; accordingly, the more affordable ICT test is more commonly used in less economically developed regions [32], which may partially explain the occurrence of cold spots in regions outside of the Pearl River Delta. Urgent calls for health systems to adopt NAAT will need to be backed by more public investment in laboratory capacity and technician trainings. Beyond test choice, uneven laboratory capacity across regions may also affect case capture, as counties with fewer labs face more barriers to reporting including sample transport and reporting delays. We attempted to account for these effects by adjusting our model estimates with annual cumulative laboratory counts in all statistical analyses, though it is an inadequate measure of the myriad other factors that dictate timely and complete reporting including staffing, training, and infrastructure. Additionally, the passive nature of the case report system occludes any insights regarding the number total number of tests conducted, as only those diagnosed and reported are included in the database. Though increases in population-level interest and awareness about STI testing are possible, the general dearth of STI health promotion outside of key populations and the lack of clinical screening guidelines suggests that these changes may be modest. Future efforts to capture this information could involve tracking the number of chlamydia tests ordered or the number of chlamydia labs ordered in sentinel clinics or laboratories. Finally, as a geospatial analysis of Guangdong the absence of data from Hong Kong is a considerable limitation given the daily volume of economic and social exchange taking place across the Hong Kong-mainland border, particularly with the city of Shenzhen with which Hong Kong shares a border and which may play a role in Shenzhen's outsized overall caseload (Fig. 1) [33].

In conclusion, we found that chlamydia case occurrence in Guangdong province has been accelerating over the past 11 years and that its expansion is likely tied to indicators of social and economic development. Past recommendations for chlamydia control in China have focused on better integration of STI care into HIV services [34]. But the prevalence of infection in populations disconnected from HIV prevention and evolving sexual norms among younger Chinese adults underscore the need for a more population-based chlamydia control strategy. The population screening recommendations of higher income settings provide a useful model, though adoption of these approaches will need to consider the comparatively low sexual health awareness of younger Chinese adults, not to mention the mixed success of these clinic-based programs to identify adequate numbers of cases [35]. In light of these patterns China may do well to revisit several facets of its own history of successful near-eradication of STIs, including women's rights promotion, mass health campaigns, and destigmatization of disease [17]. Careful population-based measures

of disease incidence will also need to be a cornerstone in the design of future population-based interventions.

Declaration of Competing Interest

We declare that we have no conflict of interest.

Author contributions

MKS, CW, PZZ, and BY all had full access to the data. MKS, KMS, ER, CW, YWY, and PZZ were involved in study design, analysis of data, interpretation. All authors were involved in interpretation of the data and either drafting or revising the final report.

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This was an unfunded study using routinely collected public health data maintained by the Dermatology Hospital of the Southern Medical University.

Data sharing

The datasets analyzed in this report are not publicly available because the data are owned by third parties. Permission to access these data can be requested through inquiries to the Dermatology Hospital of the Southern Medical University in China.

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