




# BMJ Open Rapid increase of gonorrhoea cases in Guangdong Province, China, 2014–2017: a review of surveillance data

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## ABSTRACT

**Objectives** An increased trend in the number of reported gonorrhoea cases has been observed between 2014 and 2017 in China. This study aims to describe the reported epidemic of gonorrhoea and potential driving forces in Guangdong Province, China.

**Design** A review of surveillance data.

**Participants** Three different sources of data from Guangdong Province were analysed: gonorrhoea cases reported to the Chinese sexually transmitted infections (STI) case report system (CRS); a clinic-based retrospective study conducted to collect information on annual gonorrhoea screening coverage and data from the Guangdong governmental sentinel surveillance network (SSN) to examine the gonorrhoea prevalence among males attending STI clinics.

**Outcome measures** Reported incidence of gonorrhoea, number of reported gonorrhoea cases, number of screening tests for gonorrhoea and gonorrhoea prevalence.

**Results** The STI CRS data showed that the reported incidence of gonorrhoea has increased rapidly from 15.7 cases per 100 000 population in 2014 to 27.3 cases per 100 000 in 2017 in Guangdong ( $p < 0.001$ ). Regions with a reported incidence of gonorrhoea cases of more than 10 cases per 100 000 expanded from 7 cities in 2014 to 13 cities in 2017. The SSN data showed that the gonorrhoea prevalence among males attending STI clinics increased from 2.7% in 2015 to 3.6% in 2017 ( $p = 0.14$ ). The retrospective study showed that the increased rate of screening for gonorrhoea between 2014 and 2017 was 35.0%, which was much lower than the increased rate of the number of reported gonorrhoea cases (123.3%).

**Conclusions** The number of gonococcal infections is rapidly rising in Guangdong, China. Expanded screening coverage, use of more sensitive diagnostics and increase of gonorrhoea prevalence are three potential contributors to the epidemic. Additional targeted intervention strategies are necessary in the future to control the epidemic.

## INTRODUCTION

Gonorrhoea continues to be a major public health concern in many settings because of the high incidence and antimicrobial resistance.<sup>1–3</sup> The WHO estimated that in 2012, there were 78 million cases among adults aged 15–49 years worldwide with a global incidence

## Strengths and limitations of this study

- This is one of very limited studies analysing potential driving forces of an increase trend in the number of reported gonorrhoea cases between 2014 and 2017 in China.
- Our study examined the multiple aspects of the gonorrhoea epidemic by analysing data from three different sources.
- The number of reported gonorrhoea cases might be underestimated based on a large number of private clinics that do not report gonorrhoea cases in China.
- This study was conducted in Guangdong, one of the most economically developed provinces in China; therefore, generalisability is a limitation of this study.

rate of 19 per 1000 females and 24 per 1000 males.<sup>4</sup> Gonorrhoea infection is a leading cause of infertility, pelvic inflammatory disease and ectopic pregnancy. Additionally, gonorrhoea is known to increase transmission and acquisition of HIV by inducing the production of cytokines, chemokines and defensins to modulate HIV infection and infectivity.<sup>15–7</sup>

The number of reported gonorrhoea cases gradually declined in China from 2000 to 2013, based on the Chinese sexually transmitted infections (STI) case report system (CRS).<sup>8</sup> This official STI CRS is a vital reference for STI control policy making, although repeated or erroneous reporting cases exist. However, there has been a recent reversal of this trend with a nearly 30% increase, from 7.2 cases per 100 000 in 2014 to 10.1 cases per 100 000 in 2017.<sup>9</sup> An increasing trend was also observed in several other countries, including the USA,<sup>10</sup> the UK,<sup>11</sup> France,<sup>12</sup> Australia and Greenland.<sup>13</sup> Multiple factors including greater screening coverage, use of more sensitive diagnostics and high levels of unsafe sexual behaviour among certain subpopulations were likely contributors.<sup>14–16</sup>



However, there has been limited analysis of this trend in China to confirm the increase and the driving forces to date, which is critical to informing the design of tailored intervention programme.

To address this gap, we conducted this study in Guangdong Province. We selected this province because of a high burden of gonorrhoea,<sup>9</sup> and a strong case reporting system.<sup>17</sup> In 2017, the total burden of gonorrhoea in China was 10.1 cases per 100 000 population with Guangdong province reporting 27.3 cases per 100 000 population.<sup>9</sup> Guangdong has consistently ranked among the top three provinces with a high incidence of reported gonorrhoea cases and ranking first on the number of newly reported gonorrhoea cases in China in the last decade.<sup>8 9</sup> Additionally, Guangdong has the most complete and effective surveillance system for STI among all the provinces in China<sup>17</sup> and is able to provide high-quality surveillance data.

This study aims to describe the reported epidemic of gonorrhoea in Guangdong, China, and potential driving forces of the increasing.

## METHODS

To investigate the reasons for the increasing gonorrhoea epidemic in Guangdong Province, we analysed data from three sources. First, we examined data from 2004 to 2017 from the Guangdong Provincial STI CRS to describe the gonorrhoea epidemic. Second, we conducted a clinic-based retrospective study to explore the role of expanding screening coverage on the increasing trend for gonorrhoea between 2014 and 2017. Third, we analysed the data from the Guangdong governmental sentinel surveillance network to determine whether gonorrhoea prevalence among males attending STI clinics increased between 2014 and 2017. The detailed information for these three different data sources is described below (online supplementary figure 1).

### Guangdong provincial STI CRS

The STI CRS was initiated by the Chinese Center for Disease Control and Prevention in 1985, and aims to survey syphilis, gonorrhoea, *Chlamydia trachomatis*, *Condyloma acuminata* and genital herpes across the country. The Guangdong Provincial STI CRS comprises 3261 governmental health facilities within the 21 municipalities of Guangdong Province. In all health facilities (which include STI clinics, designated dermatovenereology centres, gynaecology and genitourinary clinics, maternity and children's hospitals and other health-care entities) covered by this system, newly diagnosed STI cases are required to be reported to the STI CRS by each facility. Doctors or their assistants complete a standardised STI reporting card with socio-demographic (identification number, date of birth, sex, marital status, address and occupation), clinical (diagnostic evidence, and the onset of symptoms, diagnosis and death) and epidemiological information (transmission route). As of

2005, STI case-reporting transitioned from paper reports to electronic online submissions in China. According to national guidelines,<sup>18</sup> gonorrhoea cases are defined by positive diagnostic tests of sputum smear, culture or nucleic acid; history of sexual risk and characteristic clinical manifestations. We extracted data between 2004 and 2017 from the Guangdong Provincial STI CRS in this study.

### Clinic-based retrospective study

A clinic-based retrospective study was conducted to collect information from January 2014 to December 2017 on annual gonorrhoea screening coverage, the proportion of different types of gonorrhoea testing methods including smear, culture, PCR and immunofluorescence, and the proportion of gonorrhoea cases detected by the above four testing methods. We selected hospitals for this study according to the following procedures. First, we extracted data from the Guangdong provincial STI CRS on the number of reported gonorrhoea cases of each city in Guangdong from 2014 to 2017. The cities with a higher rate of increase in the number of reported gonorrhoea cases between 2014 and 2017 than that of Guangdong province as a whole were selected for this study. Finally, within each city, the hospitals with a higher rate of increase in reported gonorrhoea cases between 2014 and 2017 than that of the city were then selected. A total of 10 cities (Shenzhen, Guangzhou, Foshan, Zhuhai, Zhongshan, Jiangmen, Dongguan, Huizhou, Jieyang and Meizhou) and 40 public hospitals were finally selected in the study. Trained interviewers contacted the hospitals and completed a questionnaire by transcribing all existing medical records with the assistance of staff members from Information section.

### Guangdong governmental sentinel surveillance network

To increase the accuracy and reliability with which gonorrhoea incidence could be assessed, a governmental sentinel surveillance network comprising 10 STI clinics in 10 cities (Zhuhai, Dongguan, Foshan, Jiangmen, Qingyuan, Shaoguan, Jieyang, Shantou, Maoming and Zhaoqing) with a high burden of gonorrhoea was established in 2015 (online supplementary figure 2). A serial cross-sectional survey was routinely conducted in these sites among males attending STI clinics aged at least 15 years old from April to June of each year. A standardised survey protocol designed by the Guangdong Provincial Centre for STI Control was sent to these sites for data collection and management. A minimum sample size of 200–250 participants was required for each site.<sup>16</sup> After providing verbal informed consent, those who agreed to participate in the study were referred to a separate, quiet room to complete a questionnaire including demographic, behavioural and clinical information with the help of a research assistant. Urine samples were collected from all eligible participants for gonorrhoea testing by nucleic acid amplification tests.

### Statistical analysis

Measures derived from the Guangdong provincial STI CRS data included: (1) the reported incidence of gonorrhoea which was calculated by dividing the number of newly diagnosed gonorrhoea cases by the total population of Guangdong province in a specified year; (2) the average yearly rate of increase in incidence which was calculated as a geometric mean by the use of the following formula:  $(\text{incidence at years } n \text{ divided by incidence at years } m)^{1/[n-m]} - 1$ . Guangdong provincial population data were obtained from the Guangdong Bureau of Statistics of China.<sup>19</sup>

Measures for the clinic-based retrospective study included: (1) the average yearly rate of increase in the number of screening tests for gonorrhoea (see above); (2) the increased rate of screening amount for gonorrhoea between 2014 and 2017 which was calculated by the following formula:  $([\text{screening amount during year 2017} - \text{screening amount during year 2014}] / \text{screening amount during year 2014}) * 100\%$  and (3) the rate of increase in the number of reported gonorrhoea cases between 2014 and 2017 (see above).

We calculated gonorrhoea prevalence from the Guangdong governmental sentinel surveillance network data, which refers to the total number of gonorrhoea cases divided by the total population of Guangdong province in a specified year.

We used the  $\chi^2$  trend test to assess trends over years. Multivariable logistic regression was applied to examine the factors associated with gonorrhoea infection among males attending STI clinics between 2015 and 2017.

All analyses were conducted using SAS V.9.4 statistical software.

### Patient and public involvement

The participants were not involved in the development of the research question, outcome measures, design, recruitment and conduct of this study.

## RESULTS

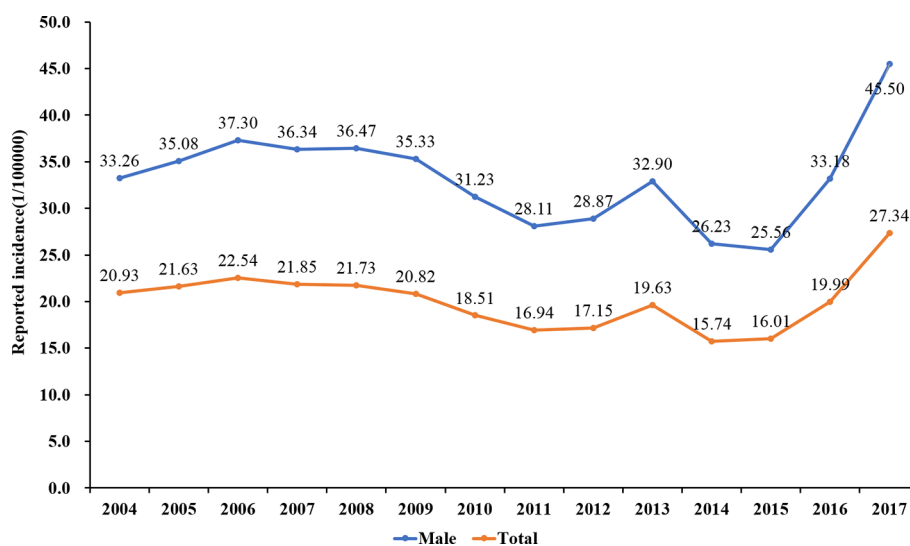
### Data from Guangdong provincial STI CRS

A total of 85 671 gonorrhoea cases were reported in Guangdong Province between 2014 and 2017. The male-to-female ratio of gonorrhoea cases decreased from 6.6 in 2014 to 6.5 in 2017 ( $\chi^2=607.11$ ,  $p<0.001$ ). While incidence decreased from 2004 to 2014, the reported incidence of gonorrhoea grew rapidly with an average yearly increase of 20.2% from 15.7 cases per 100 000 in 2014 to 27.3 cases per 100 000 in 2017 ( $\chi^2=4133.81$ ,  $p<0.001$ ), which is similar to the trend in reporting incidence of male gonorrhoea cases (figure 1). In 2014, only seven cities located in the Pearl River Delta (Shenzhen, Foshan, Zhuhai, Zhongshan, Guangzhou, Dongguan and Jiangmen) had a reported incidence of gonorrhoea over 10 cases per 100 000. In 2017, this epidemic was extended to an additional city in the Pearl River Delta (Huizhou), as well as four cities in the northern Guangdong (Qingyuan, Yunfu, Shaoguan and Heyuan), and one city in the eastern region (Shantou) (online supplementary figure 3).

### Data from a clinic-based retrospective study

The clinic-based retrospective study showed that the number of screening tests for gonorrhoea increased from 155 747 in 2014 to 210 238 in 2017 ( $p<0.001$ ), with an average yearly increase of 10.5%. Among the five different testing methods for gonorrhoea, the number of PCR tests grew most rapidly with an average yearly increase of 39.9% from 10 792 (6.9%) in 2014 to 29 543 (14.1%) in 2017 ( $p<0.001$ ), followed by culture testing with an average yearly increase of 13.5% from 42 172 (27.1%) in 2014 to 61 675 (29.3%) in 2017 ( $p<0.001$ ). Overall, the smear test was the most frequently used among the five different testing methods between 2014 and 2017.

The proportion of gonorrhoea cases detected by PCR increased from 11.3% to 12.9% between 2014 and 2017 ( $p=0.57$ ). This was similar to the immunofluorescence test, which increased from 1.5% to 4.5% ( $p<0.001$ ). By



**Figure 1** Reported incidence of gonorrhoea from 2004 to 2017 based on the sexually transmitted infections case report system.

**Table 1** Screening amount and positive gonorrhoea cases detected in the 40 hospitals, 10 cities from 2014 to 2017, a retrospective study

Test method	2014	2015	2016	2017	$\chi^2$ (p)
<b>Smear*</b>					
No. of tests (%)	88 879 (57.1)	76 202 (44.4)	74 784 (40.8)	97 774 (46.5)	3607.0 (<0.001)
No. of positive cases (%)	2389 (48.0)	2546 (46.1)	3185 (42.4)	5005 (44.6)	824.2 (<0.001)
<b>Culture*</b>					
No. of tests (%)	42 172 (27.1)	67 137 (39.2)	72 031 (39.3)	61 675 (29.3)	22.5 (<0.001)
No. of positive cases (%)	1948 (39.2)	2339 (42.3)	3262 (43.5)	4267 (38.0)	470.5 (<0.001)
<b>PCR*</b>					
No. of tests (%)	10 792 (6.9)	12 568 (7.3)	18 235 (9.9)	29 543 (14.1)	6203.5 (<0.001)
No. of positive cases (%)	564 (11.3)	573 (10.4)	818 (10.9)	1445 (12.9)	0.3 (0.57)
<b>Immunofluorescence*</b>					
No. of tests (%)	13 904 (8.9)	15 549 (9.1)	18 384 (10.0)	21 246 (10.1)	270.2 (<0.001)
No. of positive cases (%)	74 (1.5)	70 (1.3)	239 (3.2)	503 (4.5)	299.2 (<0.001)
<b>Total*</b>					
No. of tests (% , increased rate compared with 2014)	155 747	171 456 (10.1)	183 434 (17.8)	210 238 (35.0)	4525.4 (<0.001)
No. of positive cases	4975	5528	7504	11 220	1318.1 (<0.001)
No. of reported cases (% , increased rate compared with 2014)†	3600	3910 (8.6)	5627 (56.3)	8040 (123.3)	4133.8 (<0.001)

\*These data for the 10 cities were obtained from the retrospective study.

†These data for the 10 cities were from STI CRS.

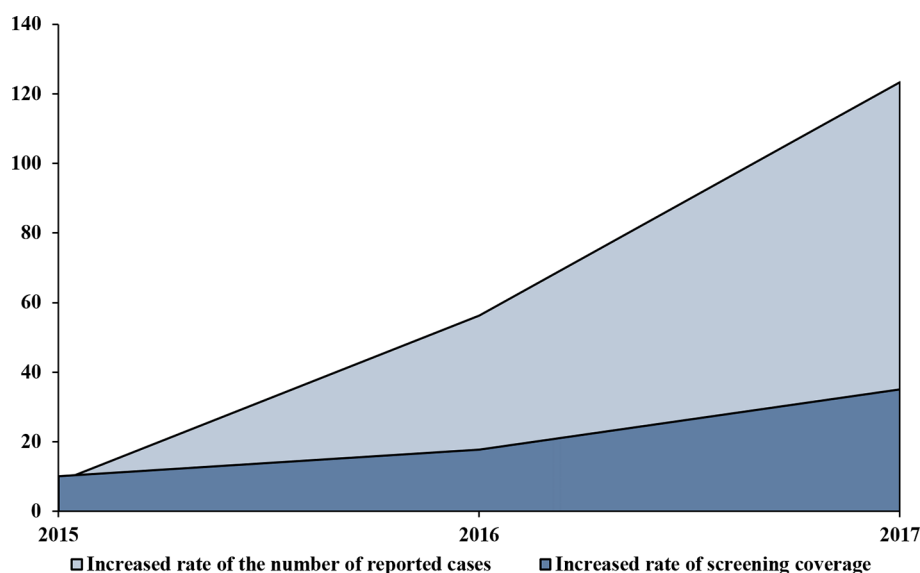
contrast, the proportion of gonorrhoea cases detected by the smear declined from 48.0% in 2014 to 44.6% in 2017 ( $p<0.001$ ), and by the culture declined from 39.2% in 2014 to 38.0% in 2017 ( $p<0.001$ ).

The rate of increase in the number of screening tests for gonorrhoea during the period from 2014 to 2017 was 35.0%, which was much lower than the increased rate

of the number of reported gonorrhoea cases (123.3%) during that time period (table 1 and figure 2).

#### Data from the Guangdong governmental sentinel surveillance network

Under the sentinel surveillance network programme, a total of 5440 participants were recruited, interviewed and

**Figure 2** The yearly increased rate of screening coverage from the retrospective study and the number of reported cases from the sexually transmitted infections case report system based on 2014 in the 40 hospitals, 10 cities.



**Table 2** Sexual risk behaviour among male attending sexually transmitted infections (STI) clinics between 2015 and 2017

	2015 (n=1749)		2016 (n=1718)		2017 (n=1973)		$\chi^2$ (p)
	N	%	N	%	N	%	
Age							1.31 (0.25)
11–20	99	5.7	50	2.9	85	4.3	
21–30	453	25.9	406	23.6	495	25.1	
31–40	444	25.4	431	25.1	543	27.5	
41–50	392	22.4	442	25.7	417	21.1	
51–60	195	11.1	215	12.5	231	11.7	
>60	166	9.5	174	10.1	202	10.2	
Marital status							1.10 (0.29)
Never married	386	22.1	405	23.6	405	20.5	
Married/engaged	1332	76.1	1266	73.7	1534	77.8	
Separated/divorced/ widowed	31	1.8	47	2.7	34	1.7	
Residency							21.3 (<0.001)
Guangdong	1614	92.3	1482	86.3	1723	87.3	
Out of Guangdong	135	7.7	236	13.7	250	12.7	
Had sex with female sex workers in the past 3 months							13.99 (0.002)
Yes	432	26.2	512	30.9	633	32.1	
No	1214	73.8	1147	69.1	1336	67.9	
Had sex with casual partners in the past 3 months							24.86 (<0.001)
Yes	288	17.5	460	27.3	490	24.9	
No	1357	82.5	1223	72.7	1478	75.1	
Recreational drug use							3.13 (0.08)
Yes	9	0.5	3	0.2	4	0.2	
No	1684	99.5	1702	99.8	1969	99.8	
Had anal intercourse with male partners							1.43 (0.23)
Yes	52	3.1	47	2.8	48	2.4	
No	1633	96.9	1657	97.2	1920	97.6	
Gonorrhoea							2.18 (0.14)
Yes	48	2.7	59	3.5	70	3.6	
No	1701	97.3	1640	96.5	1863	96.4	
Syphilis							1.05 (0.31)
Yes	60	3.5	54	3.9	73	4.1	
No	1677	96.5	1326	96.1	1699	95.9	
Chlamydia							1.24 (0.27)
Yes	106	6.1	147	8.7	137	7.1	
No	1641	93.9	1552	91.3	1796	92.9	

tested between 2015 and 2017. The gonorrhoea prevalence among males attending STI clinics increased with a yearly average of 14.94%, from 2.7% in 2015 to 3.6% in 2017, although this increase was not significant ( $p=0.14$ ). The proportion of male STI clinic attendees reporting having sex with female sex workers in the past 3 months grew significantly from 26.2% in 2015 to 32.1% in 2017 ( $p=0.002$ ). The same trend was also observed for the proportion of participants having sex with casual partners

in the past 3 months from 17.5% in 2015 to 24.9% in 2017 ( $p<0.001$ ) (table 2).

In the multivariable model adjusted for age, marital status and residency, two factors were positively associated with gonorrhoea infection: having sex with female sex workers in the past 3 months (aOR: 2.55, 95% CI: 1.89 to 3.45) and having sex with casual partners in the past 3 months (aOR: 1.49, 95% CI: 1.08 to 2.07) (table 3).

**Table 3** Factors associated with gonorrhoea infection among males attending clinics between 2015 and 2017

Characteristics	n (%)	Crude model	Adjusted model†
		OR (95% CI)	OR (95% CI)
Had sex with female sex workers in the past 3 months			
Yes	1585 (30.2)	2.59 (1.92 to 3.50)*	2.55 (1.89 to 3.45)*
No	3661 (69.8)	Ref.	Ref.
Had sex with casual partners in the past 3 months			
Yes	1216 (23.2)	1.59 (1.16 to 2.21)*	1.49 (1.08 to 2.07)*
No	4022 (76.8)	Ref.	Ref.
Recreational drug use			
Yes	16 (0.3)	1.94 (0.26 to 14.76)	1.73 (0.23 to 13.26)
No	5296 (99.7)	Ref.	Ref.
Had anal intercourse with male partners			
Yes	147 (2.8)	1.24 (0.46 to 3.39)	1.44 (0.52 to 3.98)
No	5151 (97.2)	Ref.	Ref.

\*P&lt;0.01.

†Adjusted model was adjusted for age (continuous), marital status and residency.

## DISCUSSION

A rapid increase in the number of reported gonorrhoea cases has been observed since 2014 in China. This study applied multiple sources of surveillance data from Guangdong province to identify the reasons. Our data suggest that expanded screening coverage, use of more sensitive diagnostics and increase in gonorrhoea prevalence are three potential contributors to the epidemic. Findings from this study provide insights for the design of tailored gonorrhoea intervention programme in China.

Our study found that the reported incidence of gonorrhoea in Guangdong has been increasing since 2014, and the number of cities with a reporting incidence of gonorrhoea more than 10 cases per 100 000 expended from 7 in 2014 to 13 in 2017 across Guangdong Province based on the provincial STI CRS. This increasing epidemic was similar to the epidemic across China, as well as that of many other countries, such as an 18.5% rise between 2015 and 2016 in the USA,<sup>10</sup> and a 22% rise between 2017 and 2016 in the UK.<sup>11</sup> Data from the Guangdong governmental sentinel surveillance network echoed this increasing trend among males attending STI clinics from 2015 to 2017.

Results from the clinic-based retrospective study indicated that gonorrhoea screening uptake levels have been rising with a yearly increase of 10.52% from 2014 to 2017, especially with the increased use of PCR which is the most sensitive test for *Neisseria gonorrhoea*.<sup>20</sup> Similar increases due to growing PCR use were also observed in several European countries.<sup>13 21</sup> In China, this increase can be largely attributed to the Zero Mark-up Drug policy launched by the Chinese government in 2009<sup>22</sup> and piloted in all county level public health facilities throughout Guangdong in 2013.<sup>23</sup> The Zero Mark-up Drug policy mandates that all drugs must be sold with

no markup from wholesale to retail price in all public health facilities.<sup>24</sup> According to our previous qualitative study with physicians,<sup>25</sup> this policy led to changes in diagnostic behaviours of doctors for gonorrhoea, such as increasing reliance on laboratory analysis over syndromic approaches.<sup>26</sup> For example, prior to the implementation of this policy, physicians reported typically diagnosing male patients with gonococcal urethritis based on symptoms without conducting laboratory testing.<sup>27</sup> After the policy was launched, physicians chose to provide laboratory testing to all male patients with urethral discharge for the diagnosis. This policy likely caused a rapid increase in the number of screening tests conducted for gonorrhoea in public health facilities.

While the screening coverage for gonorrhoea increased considerably between 2014 and 2017, we found that the rate of increase in gonorrhoea screening was much lower than the rate of increase in the number of reported gonorrhoea cases. Additionally, data from the governmental sentinel surveillance network indicated that the proportion of males attending STI clinics engaging in risky sexual behaviour has also grown rapidly since 2015, which is an important factor relevant to the spread of STI.<sup>28</sup> These results suggest that there was an increase in the population prevalence of gonorrhoea even if screening levels were not considered.

Our study has several limitations. First, only public health facilities are mandated to report STI in Guangdong Province. The number of reported gonorrhoea cases is likely underestimated based on a large number of private clinics that do not report gonorrhoea cases to the STI CRS.<sup>29</sup> Second, the Guangdong sentinel surveillance network only surveys males attending STI clinics, but not female attendees. Nevertheless, the trend of the incidence rate of male gonorrhoea cases can be used to

represent gonorrhoea cases overall in Guangdong. Third, there may have selection bias induced by non-response for the survey of sentinel surveillance network. Fourth, this study was conducted in Guangdong, one of the most economically developed provinces in China. We are uncertain whether the results can be generalised to other province in China. However, this study provides insights on contributing factors to the gonorrhoea epidemic and for gonorrhoea prevention at the provincial level.

## CONCLUSIONS

In conclusion, the number of gonococcal infections is rapidly rising in Guangdong, China. We used data from multiple sources to explore reasons for this increase. Expanded screening coverage, use of more sensitive diagnostics and increase of gonorrhoea prevalence are three potential contributors to the epidemic. Considering this increase in the number of gonorrhoea cases between 2014 and 2017 coincided with decreasing susceptibility of *N gonorrhoea* to currently available antimicrobial drugs,<sup>30–34</sup> prevention of gonorrhoea remains a major public health priority in China. More targeted intervention strategies and efforts, such as early detection and screening strategies, partner management, development of new diagnostics and novel treatment options, should be paid more attention in the future.

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**Data availability statement** Data are available upon reasonable request.

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