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The association between human perceived heat and primary and secondary syphilis and its variance: Results from a Case-report System

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Abstract

Background—The relationship between temperature and syphilis is poorly understood. We examined the association between human perceived temperature and the relative risk of primary and secondary syphilis, as well as these relationships across social-economic status and age groups.

Methods—Information regarding primary and secondary syphilis cases reported to the Chinese Case Report System between 2005-2013 from Guangdong province was analyzed in this study. Weather data were obtained from the National Meteorological Information Center. Distributed lag nonlinear models were applied to assess the relationship between humidex and the relative risk of primary and secondary syphilis. Results were further stratified by social-economic status and age groups.

Results—The relative risks of primary and secondary syphilis mainly increased with increased humidex, and were elevated when the humidex was around 30 or greater than 38. The humidex-RR association for the 15-40 age group was similar to the scenario pooled across the age groups, particularly in the Pearl-River Delta Region. The relative risk of syphilis in the elderly for the non-Pearl-River Delta Region did not show a clear change with humidex, whereas that in the Pearl-River Delta Region substantially increased, particularly when humidex was above 25.

Conclusion—Human perceived temperature was positively related to the relative risk of primary and secondary syphilis. People in the Pearl-River Delta Region tended to be more sensitive, with relative risk elevated at potential comfortable times or under excessive heat conditions. The vulnerability of the elderly in the Pearl-River Delta Region is concerning.

Keywords

Human perceived temperature; primary and secondary; syphilis; association; cumulative effect

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Competing interests

We declare that we have no conflicts of interest.

Introduction

In 2013, Tan et al. detected a significant annual oscillating trend in the incidence of adult syphilis in Guangdong^[1]. The periodic trend was similar to the seasonality of temperature, suggesting a potential association between syphilis incidence and temperature. Another study from Jiangsu found similar spatial patterns for syphilis and temperature, also suggesting that temperature might be a “supporting variable” for the transmission of syphilis^[2]. However, from a quantitative view, is the risk of syphilis really relevant to temperature? If so, what is the magnitude of this association?

Previous studies have also suggested that developed areas more likely to be affected by sexually transmitted diseases such as syphilis, because those areas tended to be more densely populated, with better socio-economic status as well as more social contacts among citizens^[3-5]. In addition, people of different ages differ as a function of testosterone level and sexual behaviors. Normally, citizens between 14 and 40 years old are more sexually active than those from other age groups^[6, 7]. However, does citizens' vulnerability to syphilis vary across demographic subgroups of the population?

China presents a unique opportunity to examine these knowledge gaps, which are particularly important for devising syphilis prevention and control strategies. Although syphilis had been eliminated from China in the 1960s by making free screening and treatment available to all, it has made a precipitous resurgence and now ranks among the top three reported notifiable diseases in China, particularly in Guangdong^[8-10]. Guangdong is one of the most affected areas in China, and the single province of Guangdong reported more syphilis cases than all of the countries in the European Union combined in 2008^[11].

Using information from this severely affected area, the present study aimed to assess the association between temperature and syphilis incidence. We also aimed to evaluate possible differences in this association across demographic subgroups, including social-economic status and age ranges.

Materials and methods

Study setting

Guangdong is one of the biggest provinces in Southern China, with a population up to 104 million (based on 2010 census data). According to the characteristics of the natural landscape and social-economic development, Guangdong province can generally be divided into two parts: The Pearl River Delta Region (9 cities) and the Non-Pearl River Delta Region (12 cities). According to Statistical Yearbooks for Guangdong, the Pearl River Delta Region has a higher level of social-economic development, accounting for 80% of the GDP in Guangdong Province, with less than 50% of the population^[18].

Data acquisition

Syphilis data were obtained from Chinese Case Report System (CRS) developed by the Chinese CDC^[19]. According to the Diagnostic criteria for syphilis as established by the Chinese Ministry of Health^[19], primary and secondary syphilis cases were defined as

positive for both treponemal and non-treponemal tests in addition to clinical manifestations and sexual risk history. Information including age, ZIP code, onset times and case type (stage) was entered into the CRS. Primary and secondary syphilis cases who were 15 years or older were included in this study, as they are early-stage syphilis cases, and are more likely to be related to recent exposure and transmission [17].

Weekly meteorological data were obtained from the National Meteorological Information Center (<http://cdc.nmic.cn/>). Data from meteorological stations of the same region (i.e., the Pearl-River Delta/Non-Pearl-River Delta regions in stratified analyses and the whole province when analyzed as a whole) were then averaged. According to previous studies, the same temperature can produce substantially different effects on human feelings, behaviors or even activity of pathogens under different humidity conditions [15, 16, 20-22]. Therefore, we used a humidity-adjusted temperature indicator, humidex, instead. Humidex combines the effects of humidity and temperature. It is unitless but equivalent to dry temperature in degrees Celsius. For example, if the temperature is 30°C, and the calculated humidex is 40, this indicates that the humid heat feels approximately like a dry temperature of 40°C [23]. In the present study, humidex was calculated on the basis of relative humidity and temperature using a calculator provided by CSGNetwork (<http://www.csghnetwork.com/>) in California, USA.

Statistical analysis

The nonlinearity of associations between temperature and human health outcomes is well documented [12-14]. Similarly, we can assume nonlinear relationships between relative risk of syphilis and temperature in the present research. In addition, incubation of primary and secondary syphilis, which normally lasts a few weeks or even a few months, makes the quantification of delayed temperature effects necessary for exploring the relationship between them [14-16].

Therefore, in this study, distributed lag nonlinear models with quasi-Poisson distribution were applied to evaluate the association between humidex and syphilis, with weekly number of primary and secondary syphilis cases set as the dependent variable and humidex as the independent variable. The model used in this research was

$$\text{Log (number)} = \text{intercept} + \text{cb(humidex)} + \text{ns(time)} + \text{confounders}$$

where number was the weekly number of primary and secondary syphilis cases, assuming a quasi-Poisson distribution; cb(humidex) was the cross-basis for the space of the predictor and the lag dimension of weekly humidex; ns(time) was a natural spline fit to the running index of weeks to control long-term and short-term trends; holiday and the day of week were also incorporated into the model as confounders. Relative risk (*RR*) of primary and secondary syphilis was estimated over the range of humidex values, with the humidex median as the reference.

Based on previous studies, we specified the lagged effect of humidex up to 12 weeks (the minimum lag was set to 0 by default) to calculate the cumulative effect of humidex [1, 24, 25].

The degrees of freedom for ns (time) were specified within 5–10, and for both the space of the predictor and the lag dimension of weekly humidex, within 3–6. Sensitivity analyses were conducted to evaluate the robustness of evaluations and to select the “best set of parameters” according to Akaike’s Information Criterion for quasi-Poisson distributions (Q-AIC)^[16]. In our preliminary study, elevated relative risk of syphilis was observed when the humidex was between 28–32 or greater than 40, and we therefore quantified the relative risk of syphilis within high-risk ranges of humidex relative to the normal conditions. Data management and analyses were conducted with R packages including “data.table”, “ggplot2” and “dlnm”^[26–28].

Results

Overall, a total of 111,986 primary and secondary syphilis cases aged 15 years or older were identified and reported to the CRS from Guangdong province, during 2005–2013 (Table 1). The provincial incidence rate of primary and secondary syphilis was 12.58 cases per 100,000 people. The rate for the Pearl River delta region was 16.95 cases per 100,000 people, and was more than twice that for the non-Pearl River delta region (7.87 cases per 100,000; Figure 1).

Provincially, the average humidity was 77.06% (70.62%, 81.62%) and the average temperature was 23.65°C (17.59°C, 27.28°C). The average humidex was 30.54 (20.59, 38.35). Figure 2 also shows that humidex and the weekly number of primary and secondary syphilis cases share a similar seasonality.

Overall, the relative risk of primary and secondary syphilis increased with humidex (the first row of panels, Figure 3). It slightly increased when the human perceived temperature was around 15 and clearly peaked around 30. When humidex increased to 38, relative risk started to increase again and reached another peak. The relative risk of syphilis within a humidex of 28–32 was 1.96 (95% CI: 1.14, 3.35) times higher than that under normal heat conditions in the Pearl-River Delta Region. In the non-Pearl River Delta Region, the relative risk significantly elevated when humidex was beyond 38 (Table 2).

The scenario for the 15–40-year old age group was similar to that for the whole sample, particularly in the Pearl-River Delta Region. When human perceived temperature was between 28–32, the relative risk of syphilis in the Pearl-River Delta Region was 2.04 (95% CI: 1.13, 3.70), which tended to be higher than the value provincially at 1.75 (95% CI: 1.04, 2.96) or in the non-Pearl River Delta Region (1.14; 95% CI: 0.62, 2.08). The relative risk in the non-Pearl River Delta Region was significantly elevated when humidex went beyond 40 [2.23 (95% CI: 1.11, 4.50)].

There was a single peak of relative risk for the 40–65 age group in the non- Pearl River Delta Region when humidex was around 32. When humidex was approaching 40, rates again started to slightly increase. For those greater than 65 years old in this area, the relative risk did not visually increase with humidex, and actually decreased as humidex increased. However, in the Pearl River Delta Region, the relative risk of syphilis for both age groups (i.e. 40–65, > = 65) monotonically increased with increasing humidex, particularly for those

greater than 65 years old. The relative risk for the elderly substantially increased when humidex was above 25.

Discussion

With syphilis data collected from one of the most heavily affected areas in the world and covering over 100,000 cases, this study assessed the potential association between syphilis and human perceived temperature, offering a new angle on prevention of STDs. We found that the relative risk of primary and secondary syphilis (cumulated over the potential incubation) increased with human perceived temperature, but the association varied across demographic subgroups of the population. Our study represents the first quantitative temperature-STD relationship research, expanding limited literature by detecting trends in relative risk of syphilis and thresholds of human perceived temperature.

We estimated that the relative risk of primary and secondary syphilis was overall elevated when humidex was around 30, or under excessive heat conditions. Normally, conditions of temperature between 20-25 Celsius are considered to be the most comfortable for outdoor activities^[13, 16, 29]. In subtropical areas such as Guangdong, the most comfortable range of truly perceived temperature is around 30 when the high humidity in this area is taken into consideration^[16]. Therefore, humans tend to socialize more during such days. Wearing less or more revealing clothing is another reason probably related to the increase of sexual behaviors during this time^[30]. In addition, increased relative risk under excessive heat conditions, which may be associated with increased testosterone levels which may cause more fidgets and sexual activities, was also expected^[1]. Another potential factor that contributes to the elevated relative risk of sexually transmitted diseases during excessively hot days is that employees often receive extra bonuses such as the High Temperature Allowance and thus have more money available on these days. We also found a slight increase in the relative risk of syphilis when human perceived temperature was around 15. Looking into the original weather data, we found that this pattern was basically happening during December and early January. The relative risk during this period should be relatively low, and Christmas and New Year holidays probably played an important role in increasing the relative risk of primary and secondary syphilis.

This study demonstrated that the humidex-RR association for cases between 15-40 years old have dominated the provincial scenario. One potential reason for this phenomenon is that people in this age range tended to be sexually active, have a greater chance of engaging in high-risk sexual behaviors, and account for a large proportion of reported cases^[4, 31, 32]. Among this age group, we found that people in the Pearl River Delta Region were more sensitive to humidex conditions around 30. Two factors could be evoked to explain this phenomenon. First, the Pearl River Delta Region is more developed in terms of infrastructure and public transportation, which could facilitate outdoor activities. There are also a large number of migrants in this area who may be living without family and, as a result, attending more activities with their peers or having sexual partners other than their spouses^[33, 34]. Previous studies have shown that this is a very important determinant of STD transmission in this area^[35, 36]. Second, there are more entertainment avenues in the Pearl River Delta region, which creates more chances for high-risk sexual behaviors.

In the present study, the relative risk of primary and secondary syphilis for the elderly in the non Pearl River Delta Region did not obviously change with human perceived temperature. However, the *RR* for those in the Pearl River Delta region substantially increased, particularly when the humidex was above 25. Differences in sexual activity among the elderly from these two regions is a potential explanation. The elderly from the Pearl River Delta region tended to have higher income and retirement pay. The elevated risk of syphilis of those in more developed areas may be associated with increased availability of medicines for erectile dysfunction, or older man/younger woman commercial sexual relations [17, 37, 38]. Therefore, the sexual health of the elderly in the Pearl River Delta region has become an important issue.

Our study has a couple of limitations. First, underreporting is a common issue for case report data even though real-time case-based reporting data are the best and most complete dataset currently available. Second, the incubation period of syphilis is related to various factors such as human vulnerability. Therefore, we could not know exactly the period from infection to the occurrence of typical symptoms. To get more robust estimates, we could evaluate the cumulative effect of temperature instead of lag-specific effects. Third, this study is ecological in design, and results obtained at the population level may not apply to individual situations. Future studies should further confirm these findings at the individual level.

Our results suggest the potential of meteorological angles on STD prevention strategies. The quantitative relationship between syphilis and human perceived temperature as well as thresholds identified in this study describe changes in citizens' vulnerability to syphilis related to temperature. Findings from this study, combined with weather forecasts, might contribute to an early warning system of syphilis risk. This is particularly important in the context of global climate change. Furthermore, for policy makers, future prevention strategies need to be more subpopulation-targeted.

In conclusion, human perceived temperature is positively associated with the relative risk of primary and secondary syphilis. People in the Pearl River Delta region tended to be more sensitive, with relative risk elevated at potential comfortable times or under excessive heat conditions. The vulnerability of the elderly in the Pearl River Delta region is of specific concern.

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Figure 1.
Primary and secondary syphilis burden in Guangdong, China, 2005–2013.

Figure 2.

Time series plot for weekly number of primary and secondary syphilis cases and humidex (the seasonality of primary and secondary syphilis cases is identical to that of the humidex, which suggests a positive association between primary and secondary syphilis incidence and humidex).

Figure 3.
The association between humidex and the cumulative risk of primary and secondary syphilis in Guangdong, China, 2005–2013.

Table 1

Description of the primary and secondary syphilis cases (N) and weather factors (Median (IQR)).

	Overall	Pearl-river delta region	Non-pearl river delta region
No. of Cases	111,986	78,266	33,720
Reported Incidence (per 100,000)	12.58	16.95	7.87
Median Temperature (IQR)	23.65(17.59,27.28)	23.97(18.14,27.35)	23.38(17.33,27.11)
Median Humidity (IQR)	77.06(70.62,81.62)	76.74(69.82,81.56)	77.3(71.91,81.78)
Median Humidex (IQR)	30.54(20.59,38.35)	30.89(21.24,38.52)	29.64(19.95,38.03)

Table 2

The relative risk of primary and secondary syphilis under conditions in which humidex was between 28-32 or was greater than 40 in Guangdong, China, 2005-2013

		Whole province	Pear-River Delta Region	Non-Pear-River Delta Region
Overall				
28 Humidex	32	1.61(0.99,2.61)	1.96(1.14,3.35)	1.07(0.64,1.78)
Humidex	40	1.46(0.98,2.18)	1.06(0.73,1.55)	1.98(1.08,3.65)
15<Age<=40				
28 Humidex	32	1.75(1.04,2.96)	2.04(1.13,3.70)	1.14(0.62,2.08)
Humidex	40	1.45(0.95,2.22)	1.10(0.73,1.66)	2.23(1.11,4.50)
40<Age<=65				
28 Humidex	32	1.66(0.91,3.01)	1.80(0.90,3.60)	1.08(0.54,2.16)
Humidex	40	1.73(1.05,2.86)	1.02(0.62,1.67)	2.06(0.89,4.76)
Age>65				
28 Humidex	32	0.83(0.38,1.79)	1.14(0.39,3.32)	0.76(0.32,1.79)
Humidex	40	0.91(0.47,1.75)	0.73(0.34,1.57)	1.07(0.36,3.12)