A re-analysis in exploring the association between temperature and COVID-19 transmissibility: an ecological study with 154 Chinese cities

To the Editor:

Exploring the role of ambient temperature in coronavirus disease 2019 (COVID-19) transmission is of importance in understanding the patterns of the epidemic. YAO *et al.* [1] concluded that there were no significant associations of COVID-19 transmissibility with temperature and ultraviolet (UV) radiation in 62 Chinese cities. Inspired by the nonlinear dose–response relationship between ambient temperature and influenza transmissibility explored previously [2, 3], we argue that the association between COVID-19 transmissibility and temperature might be complex in nature, which may be overlooked by a linear analytical framework. We, therefore, examined the likelihood of a nonlinear association between COVID-19 transmissibility and ambient temperature.

To quantify the COVID-19 transmissibility, we calculated R_0 for each Chinese city *via* the standard approach with a Gamma distribution having mean±SD values of 5.5±3.3 days for the generation interval [4, 5]. A total of 154 Chinese cities were detected with COVID-19 outbreaks (R_0>1) between December 2019 and February 2020, the same period studied by YAO *et al.* [1]. Our R_0 estimates for the 154 cities (15 inside Hubei and 139 outside Hubei) have a mean±SD of 1.4±0.3, which was largely consistent with the work reported by YAO *et al.* [1], where 62 Chinese cities were included (12 inside Hubei and 50 outside Hubei) [1]. The maximal R_0 was estimated at 2.5 (95% CI 2.4–2.6) in Wuhan, which is consistent with previous findings [1, 5]. We interpolated monitoring data of mean temperature and relative humidity during the same period from 689 stations to continuous rasters by ArcGIS, and then we extracted values from the rasters and linked them to the 154 selected cities.

We first used the multivariable linear regression model, the same framework with YAO *et al.* [1], and adjusted for relative humidity, to estimate the association between ambient temperature and R_0. We found the association was slightly negative but not of statistical significance (figure 1a), which is partially in line with YAO *et al.* [1] and another recent study across 100 Chinese cities [6]. Next, generalised linear regression with structural break design, *i.e.* discontinuity regression, was employed to explore the linear structural change in the relationship, in terms of the slope changes, between ambient temperature and R_0. The discontinuous point was selected based on the likelihood profile, shown in the inserted panel in figure 1b. We estimated the optimal discontinuous point at 7°C (95% CI −7.0 to 11.5°C), which is largely consistent with an emerging report across 429 cities worldwide [7]. In figure 1b, the temperature is negatively and significantly associated with COVID-19 transmissibility when it is higher than 7°C. We further remarked that a slight change in the temperature discontinuous point would not affect the results. Then, for validation of the "shape of the relationship", we attempted multivariable nonlinear regression by using the natural spline function with two degrees of freedom determined by the minimal Akaike information criterion (AIC). We set the knot of the spline regression as the discontinuous point at 7°C. The discontinuity regression model (AIC=51.78) and spline regression model (AIC=53.41) outperformed the linear regression model with smaller AICs (against the AIC of 53.82 for the linear regression). The overall nonlinear association between R_0 and temperature was of statistical significance in terms of the p-value (=0.044) from the likelihood ratio test. The negative trend was clearly observed when temperature

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In this national ecological study across 154 Chinese cities, the ambient temperature was found to have a nonlinear negative association with COVID-19 transmissibility https://bit.ly/3esw8rc

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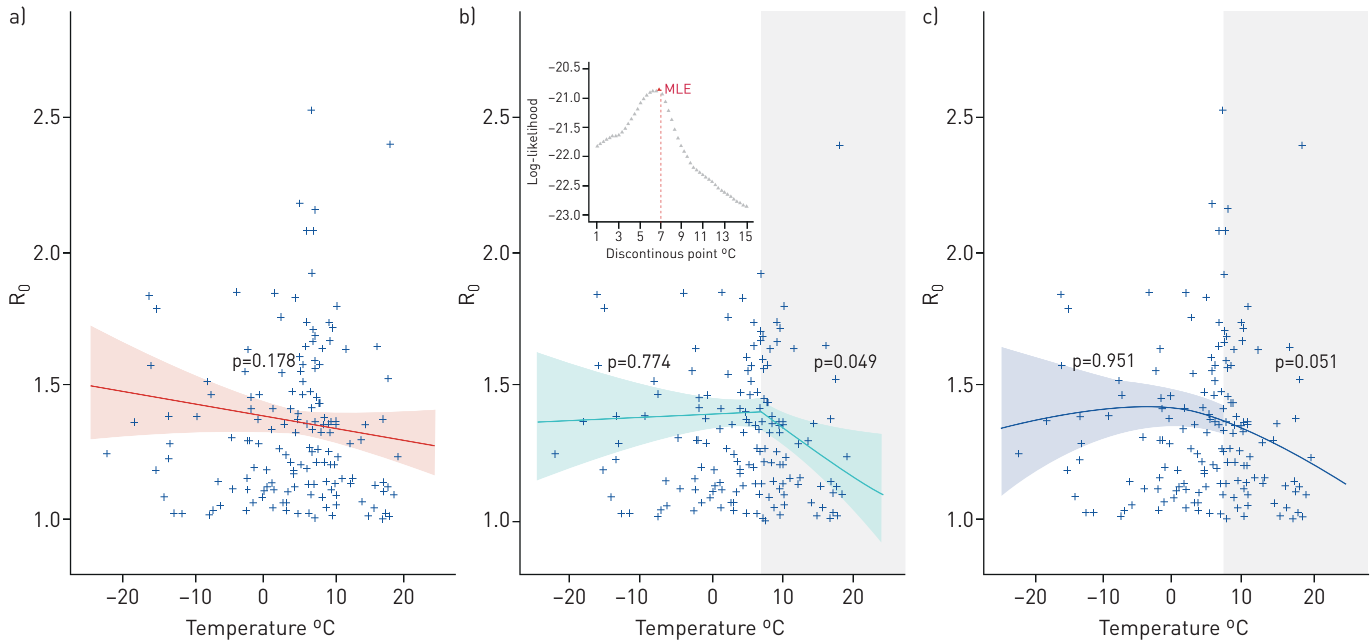

FIGURE 1 Association between temperature and coronavirus disease 2019 transmissibility (R_0) across 154 Chinese cities. a) Multiple linear regression (p=0.178; AIC=53.82). b) Linear regression with a discontinuous point at 7°C (p=0.049 when temperature is over 7°C; AIC=51.78). The inserted panel shows the likelihood profile of the discontinuous point and its maximum likelihood estimate (MLE). The red triangle is the MLE at 7°C, and the grey triangles are the input samples. c) Spline regression with a knot at 7°C (AIC=53.41). AIC: Akaike information criterion.

is higher than 7°C (figure 1c), which appears similar to the patterns of the discontinuity regression (figure 1b). We further tested the interaction between temperature and relative humidity on the COVID-19 transmissibility in the model. No clear interaction effect (or effect modification) was observed in terms of the p-values (>0.050) from the likelihood ratio test. We further adjusted for fine particulate matter ($PM_{2.5}$) in the model, and we still observed the negative trend between temperature and R_0 values when temperature was over 7°C.

Temperature could relate to viral transmissibility due to its impacts on virus viability and host immunity. Viruses are more stable at low temperature, and hosts may be more susceptible to the disease due to weakened immune protection [8]. Similar findings were also observed in extended experimental studies on other coronaviruses [9, 10]. Due to the fact that major outbreaks in China ended before April 2020, the mean temperatures were below 15°C for most Chinese cities, *i.e.* 91% and 89% of the cities in our analysis and that by Yao *et al.* [1], respectively, and 80% and 81% were below 10°C. Hence, we suspected a more evidently negative association might be observed from the COVID-19 epidemics in a warmer context.

Caution should be taken when interpreting the results. First, the temperature cut-off, *i.e.* 7°C, was selected based on the modelling process. While uncovering its practical significance is limited in the current ecological study design, we emphasised the likelihood of the structural change in the association between ambient temperature and COVID-19 transmissibility. Further studies are required for exploring and quantifying the dose–response relationship between ambient temperature and COVID-19 transmissibility in more complex contexts. Second, since the outbreak will not occur with $R_0<1$ theoretically, only sporadic cases may be observed. In this situation, a precise estimation of R_0 would be difficult, and thus only cities with $R_0>1$ were included in our analysis. This stratification may limit our conclusion within the epidemic regions. Third, the potential impact of temperature is rather restricted since the change in temperature may solely contribute to 11.2% variability of R_0, in terms of the McFadden's pseudo-R-squared. Hence, we remark that control strategies for the COVID-19 pandemic barely relying on environmental factors are unlikely to succeed. Moreover, temperate and subtropical climates dominate most of China (the hardest-hit cites lie in similar latitude). The impact of temperature on the COVID-19 transmission in tropics remains uncertain due to the heterogeneity in climate. Last, the ecological study is not enough to evidence the causal relationship because of the residual confounding by other covariates, such as social distancing and age distribution.

We suggest that the existence of an association between COVID-19 transmissibility and ambient temperature should be examined and reaffirmed with systematic and comprehensive settings, and we argue that a nonlinear association might exist, similar to that seen for influenza. Studies with longer observation periods and stronger evidences are warranted to further test and verify this.

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