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The impact of air temperature and containment measures on mitigating the intra-household transmission of COVID-19: a novel data-based comprehensive modeling analysis

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Abstract

Objectives

Because of the implementation of non-pharmaceutical interventions (NPIs) in many countries, the transmission pattern of COVID-19 was changed to intra-household or intra-acquaintance spreading. And as the second wave of the COVID-19 pandemic worldwide, it was necessarily to re-estimate the influence of temperature on COVID-19 transmission, especially on intra-household transmission.

Methods

We established a stochastic epidemiological model (susceptible-Exposed-Infected-Quarantined-Removed model (ScEIQRsh)) to simulate the intra-acquaintance or intra-household spreading pattern of COVID-19, and evaluate the influence of air temperature on COVID-19 transmission. The model was fitted by Metropolis-Hastings (M-H) algorithm, one Markov Chain Monte Carlo (MCMC) method with a cost function based on least squares method.

Results

From fitted model, the fitted transmission rate (β') of COVID-19 among acquaintances was 10.22 (IQR 8.47, 12.35) across Mainland China. The association between air temperature and the β' of COVID-19 suggests that COVID-19 pandemic might be seasonal with the optimal temperature range of 5℃-14℃ (41°F-57.2°F) and peak of 10℃ (50°F) for spreading. Model simulation also demonstrated that the measures to diminish contactable susceptible (Sc), and measures to avoid delay of diagnosis and hospitalized isolation (η) were more effective than contact tracing (κ, ρ). This study provides a new tool to assess the influence of air temperature and containment measures on COVID-19 transmissibility, which can be helpful for decision making and prediction of the COVID-19 transmission in the upcoming winter. And it suggests the necessity and urgency of vaccine for ultimate COVID-19 control.

Conclusions

This study provides a new tool to assess the influence of air temperature and NPI measures on COVID-19 transmissibility, which can be helpful for decision making of public health strategy, and suggests the necessity and urgency of vaccine for ultimate COVID-19 control.

Strengths and limitations of this study

This study provided one novel epidemiological model to mimic the intra-household transmission of COVID-19 and fitted with the epidemic data in China Mainland.

This study investigated the relationship between air temperature and the transmission rate of COVID-19 besides the influence of non-pharmaceutical interventions (NPI).

The efficiency of NPIs, especially the effect of contact tracing in mitigating the transmission of COVID-19 was studied

This study only included the epidemic date of Mainland China for model validation because we cannot access the NPIs data, e.g., close contacts of other countries.

This model could be fitted even if the NPIs data is sparse, but with less accuracy.

Introduction

COVID-19 is spreading worldwide since January 2020. The non-pharmaceutical interventions (NPIs), including physical and social distancing, quarantine, and isolation are vitally important for COVID-19, because of the so fast spreading and the subsequent insufficiency of health-care resources leading to high mortality[1]. In China, Besides the announcement of keeping physical and social distance to the public, epidemiological survey (EPS) -based quarantine and hospitalized isolation were widely implemented in all the provinces of Mainland China after the lockdown of Hubei province on the Jan 23, 2020 in emergency [2]. Even many countries implemented various interventions, including pharmaceutical and non-pharmaceutical interventions, it is still pandemic with a terrible consequence for global health currently. It's winter with low temperature again and there are a few cases of COVID-19 in China right now. What's the influence of temperature on the COVID-19 incidence and transmission besides the NPIs' effect?

The meteorological impact on COVID-19 transmission was still controversial. Wang Mao *et al* [3] and Sajadi MM *et al* [4] reported that regions in 30-50º N' corridor with 5℃-11℃ (41°F-51.8°F) average temperature had increased COVID-19 transmission, but Canelle Poirier *et al* [5] indicated no significant correlation between high temperature/ humility and COVID-19 transmission. However, none of the above studies considered the influence of NPIs in their analysis. We then used the data from China as an appropriate example to evaluate the relationship between the air temperature and COVID-19 spreading. Because, firstly, the social intervention in all the provinces of China is almost taken at the same time and is almost uniform with different intensity between provinces. Secondary, the latitude span of mainland China is large enough to reflect the zones with daily mean air temperature of -7℃ to 20℃ in winter. At last, we could get the completely data of the daily numbers of cases in quarantine by contact tracing for each province. Thus, we constructed a new kind of SEIR (Susceptible-Exposed-Infected-Removed)-based model which can separate the influence of social intervention measures from confounding factors, and with machine learning methods we achieved the precise influence of air temperature on COVID-19 spreading.

Under the effective social NPIs implemented, the spreading pattern of COVID-19 was characterized of clustered or intra-household transmission. For example, in China, a report of the "WHO-China Joint Mission on COVID-19" claimed that human-to-human transmission of COVID-19 largely occurred intra-family [6]. In Guangdong and Sichuan province, about 78%-85% of clustered infections were within families [6]. And in Beijing, there are 176 clustered cases among 262 confirmed cases and 133 (50.8%) were clustered intra-family cases [7]. The implementation of effective social NPIs would change the spreading pattern of COVID-19 into intra-acquaintance spreading. To simulate the early spreading and early social intervention, we established a novel non-classical SEIR NPIs model, named ScEIQRsh (Contactable Susceptible-Exposed-Infected-Quarantined-Removed) model to depict a new spreading pattern of COVID-19. The classical SIR or SEIR (Susceptible-Exposed-Infected-Removed) epidemic model assumes that infectors mix up with all the susceptible per day, whereas ScEIQRsh model assumes that infectors mix up with the contactable susceptible per day. The contactable susceptible indicates the family members, relatives, co-workers, friends and some contactable strangers for obtaining daily necessities of the infectors. Several studies assessed the effectiveness of NPIs, such as travel restriction [8 9], airport screening [10 11], social distancing [12], and contact tracing [13] by classical SEIR based model without consideration of influence of NPIs on the transmission property of COVID-19. We estimate the effectiveness of integrated NPIs to simulate COVID-19 restricted spreading among acquaintances for the first time.

Materials and Methods

Development of the dynamical non-classical SEIR model for COVID-19

The developed ScEIQRsh model is an expanded model from classic SEIR epidemic model, which contains six compartments named as Sc (contactable susceptible), E (the exposed to SARS-COV-2), Q (daily close contacts being in quarantine), I (infectors outside of the healthcare system), Rh (accumulative hospitalized infectors), and Rs (self-recovery individuals with asymptomatic infection or mild symptoms who have never be hospitalized and registered in healthcare system) (Figure 1; supplementary methods). Sc represents the contactable susceptible under the social NPIs, such as lockdown, social distancing, cancelling gatherings, closing public places, which is set as a random variable in the model. Q reflects the contact tracing (CCT) for quarantine, and Rh reflects the confirmed and hospitalized infectors in isolation wards, and this kind of population was daily reported by public health agency. E, I, and Rs compartments were outside of the healthcare system. Rh is really the reported cumulative confirmed cases in the model. Every compartment has been linked by a few parameters, and the flow velocity of each compartment is illustrated in figure 1 (details in the supplementary methods).

Parameters in ScEIQRsh model

The definition and initial range of model parameters of β', σ, γ, κ, ρ, ω, η and Sc in the model were listed in Table 1. β' was the transmission rate dependent of the property of SARS-COV-2. σ and γ were associated with the intrinsic incubation period and communicable period of COVID-19. κ, ρ and ω were associated with contact tracing and quarantine. η reflected the pace of confirmed diagnosis and hospitalized isolation for infectors. Other indexes could be calculated from the solved model, such as the contact rate (CR), the quality of CCT (surveyQ), the proportion of untraceable infectors (approximately equate to the asymptomatic) (utI%), the incubation period and communicable period of SARS-COV-2, and among them, CR reflects the proportion of Sc in population under the integrated NPIs, surveyQ represents the quality of contact tracing. This model can be mathematically described as five differential equations (details in the supplementary methods):

(1) $dE/dt = \beta' ScI/(Sc+E+I+Rs+Rh+\rho Q) - \kappa\eta\rho I - \sigma E$;

(2) $dI/dt = \sigma E - \eta I - \gamma I$;

(3) $dQ/dt = \kappa\eta I - \omega Q$;

(4) $dRh/dt = \eta I + \rho\omega Q$;

(5) $dRs/dt = \gamma I$;

Acquisition the epidemic data

The intra-household and clustered transmission of COVID-19 [7] could be observed at the beginning of COVID-19 spreading in Mainland China [6]. And each Provincial Health Commission would report the daily number of close contacts being in quarantine besides reporting the number of daily confirmed cases of COVID-19. This completed data of Mainland China was good for fitting the ScEIQRsh model and investigating the intra-household or intra-acquaintances transmission of COVID-19. We collected the data of daily accumulative confirmed cases of COVID-19 from January to March, 2020 through the 31 Provincial Health Commission of Mainland China. The daily number of close contacts in quarantine and the daily number of whom were relieved of quarantine were also collected from the provincial government website in China. Xizang and Qinghai province were excluded because of few cases, with only one and 18 confirmed cases, respectively. Almost all the diagnosed cases were hospitalized in isolation wards simultaneously according the Guidance, thus the reported confirmed cases were just the hospitalized infectors in China. Details of the criteria of confirmed cases and close contacts in quarantine were clarified in the supplementary methods.

Simulation and model fitting

We fitted both the reported accumulative confirmed cases and daily close contacts in quarantine with Rh and Q compartments by ScEIQRsh model for each province by Markov Chain Monte Carlo (MCMC) method with a cost function based on least squares method. Briefly, model parameters and Sc were random samplings with Metropolis-Hastings (M-H) algorithm, one of Markov Chain Monte Carlo (MCMC) method. The proposal distribution for accept-reject is a Bernoulli distribution from the comparison of the cost function of curve fitting in iteration (better or not). Both simulated curves of Rh and Q were simultaneously fitted with the raw data (the real word data) by the least-squares method, and the cost function was SSE/SST (Sum of Squares for Error/Sum of Squares for Total). The optimized parameters were documented with 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for 29 provinces of Mainland China. The expected value and standard deviation for each parameter were then confirmed.

Air temperature of provinces in China during the COVID-19 spreading

The minimum (Tmin), mean (Tmean), maximum (Tmax) air temperature of each province was collected from the National Meteorological Administration from Jan 15, 2020 to Feb 15, 2020 (one week before and three weeks later of Jan 23, 2020 (Day 0)). The LOESS regression was used to depict the relationship between the air temperature of 29 provinces and COVID-19 transmission rate in ScEIQRsh model.

Patient and Public Involvement

No patient involved

Statistical analysis

The enrolled 29 provinces for model validation were separated into seven geographical regions, named as North, Northeast, East, Central, Northwest, South and Southwest China. Both curves of Rh and Q was simultaneously fitted with the raw data by least squares method with tolerance of 1.05, and the cost function was SSE/SST (Sum of Squares for Error/Sum of Squares for Total). The data process was performed on R (version 3.6.1), and the "deSolve" R package was used as the solver of differential equations. The R source code can be found in *GitHub*. The parameters were denoted as mean±SD for each province, and the median (interquartile range, IQR: 25%, 75%) was used for describing across provinces.

Results

Fitting the COVID-19 transmission with integrated social NPIs

The ScEIQRsh model can be well fitted with both the reported number of daily accumulative confirmed cases and close contacts being in quarantine in 29 provinces of Mainland China (Figure 2, Figure S1). The predicted daily Rh and Q compartments were coincident with the provincial reported numbers. From the fitting curves, the accumulative confirmed cases reached the plateau and stop increasing within 25-30 days, which indicated that the COVID-19 transmission could be mitigated by adoption of containment measures. The median transmission rate (β') for 29 provinces were 10.22 (IQR 8.47, 12.35), which implied about 10.22 person would be infected by one infector in case that the susceptible are mostly acquaintances and Sc is extrapolated to infinite (Figure 3A, Table 2, Table S1).

The influence of air temperature on the transmissibility of SARS-COV-2

The span of mean air temperature for every province was from -15 ℃ (5 °F) to 20.25 ℃ (68.45 °F) during the COVID-19 spreading period of Jan to Feb 2020 in China (Figure 3B, C). The nonlinear association between transmission rate (β') and air temperature was depicted by LOESS fitting. As the daily air temperature increased from subzero (0℃, 32°F), the value of β' raised gradually until the air temperature went up to a peak of 7℃ (44.6°F) for minimum daily temperature, 10℃ (50°F) for mean or 15℃ (59°F) for maximum daily temperature, respectively (Figure 3D, E, F), and then declined sharply as the temperature continued to raise. We observed transmission rate (β') was higher than 11 in the range of 5℃-14℃ (41°F-57.2°F) for mean air temperature, which may be most suitable for COVID-19 spreading.

Assessment of NPI measures mitigating the spreading of COVID-19 and suppositional simulation

The second wave of COVID-19 pandemic is appearing in many countries. The containment measures are still pivotal for controlling COVID-19 spreading. We mainly assessed three independent parameters, contact rate (CR), η and surveyQ, which were crucial for stopping the spreading chain. Based on our model, the median Sc was estimated as 26.98 (IQR:13.97, 54.57) with the highest in Hubei and lowest in Neimenggu province (Table S1). The median CR for 29 provinces was accordingly 6.84E-07 (IQR 3.77E-07, 1.44E-06) (Figure 4A). To illustrate the influence of NPI measures on COVID-19 transmission for ScEIQRsh model, we arbitrarily adjusted CR, κ, ρ, and η value with representative 30% or 50% up/down-regulation to simulate the suppositional spreading situation. If CR were 30% or 50% enlarged, the eventual accumulative hospitalized cases (Rh) would strongly increase, the peak of infectors (I) would be brought backward and vice versa (Figure 4B, 4C). The median for velocity of hospitalized isolation for infectors (η) was 0.69 (IQR 0.47, 0.87) among 29 provinces, with η value greater than 0.85 in Jilin, Heilongjiang, Shanghai, Jiangsu, Hubei, Hunan, Guangxi and Guizhou province (Figure 4D). The influence of η is the opposite to CR. If the η were increased as 30% or 50%, the eventual Rh would be strongly reduced and vice versa (Figure 4E, 4F).

The κ and ρ can be used to assess the effectiveness of CCT, and the median κ of 29 provinces was 42.0 (IQR 27.83, 60.78), suggesting that 42 close contacts of one infector had been excavated averagely by CCT groups (Figure S2A). The COVID-19 positive rate (ρ) in close contacts was speculated as 0.98% (IQR 0.47%-1.60%), ranged from 0.03%-5.10% (Figure S2B), which was quite close to the WHO-China joint report of 0.9%-5% in China [6]. SurveyQ, the product of κ times ρ, was 0.39 (IQR 0.22, 0.55), which indicated that 0.39 positive cases were found in close contacts of CCT averagely for each confirmed infector (Figure 4G). In case of enlarged κ or ρ, the eventual accumulative number of confirmed COVID-19 would diminish and the plateau of Rh would be brought forward (Figure 4H, 4I, Figure S2C-S2F). On the same adjusted amount, the effectiveness of CR and η on spreading prevention were stronger than that of CCT parameters, κ and ρ.

Blind zone of contact tracing and asymptomatic infectors in NPIs strategy

With the integrated social NPIs, COVID-19 transmission mostly occurred between free infectors and acquaintances, as well as a few strangers whom the infectors have to contact for daily necessities. In a typical clustered intra-acquaintance transmission, the index case transmitted to four of his family members and one friend directly, and the friend's family indirectly infected within half a month[14] (Figure 5A). After emergency response, multiply provincial contact tracing group were established to investigate the contact history of each confirmed infectors and notified the close contacts to be in self-quarantine at home or in shelters. CCT can easily find close contacts of acquaintances, but be inefficient in finding transmission among strangers in public space. For example, a salesman index transmitted to two unacquainted salesmen in other sales areas sequentially without gathering in a large mall, and a customer without any inquiry and purchase was infected by one of the transmitted salesmen after 30-minutes lingering (Figure 5B). This transmission chain in strangers could not be easily found by contact tracing, and was only revealed after all the participants appeared symptoms (Figure 5C).

Another blind spot of contact tracing is about asymptomatic infection. Rs compartment in the ScEIQRsh model consists of the self-recovery individuals who have never be hospitalized and not registered in healthcare system mostly because of asymptomatic infection or mild symptoms. The calculated proportion of asymptomatic and mild-symptom infectors without hospitalization (the proportion of untraceable infectors, utI%) by ScEIQRsh model was 14.88% (IQR 8.17%, 25.37%), ranged from 3.92%-34.36% across 29 provinces, which implied that average 14.88% COVID-19 patients couldn't be found out with social NPIs, and the average proportion of asymptomatic in COVID-19 patients should be smaller than 14.88% (IQR 8.17%, 25.37%) (Figure 5D). The higher surveyQ of CCT can only reduce but not eliminate utI% (Figure 5E), but high η could decline the utI% constantly (Figure 5F). Hence, contact tracing is not sufficient to find all the infectors, especially in stranger-stranger transmission and asymptomatic infection. The ratio of asymptomatic infectors also influenced by air temperature. When the mean air temperature is subzero, the utI% is high (Figure 5G).

Calculation of the incubation period and communicable period of COVID-19 with ScEIQRsh model

The median incubation period was calculated with sigma and eta (incubation period $\approx 1/\sigma+1/\eta$) by this model, of 4.16 days (IQR 3.60, 4.71) (Figure S3). The communicable period of COVID-19 was infectious period related to asymptomatic and some mild-symptom infectors, with a median of 6.77 days (IQR 4.53,10.36) calculated as $1/\gamma$ (Table 2). The median time from individuals exposed to SARS-COV-2 to being contagious was 2.39 days (IQR 2.26, 2.56) determined by $1/\sigma$ (Table 2).

Discussion

COVID-19 firstly outbroke in Mainland China last winter, whether the meteorological conditions might affect the spread of COVID-19 is vitally important in prediction of COVID-19 prevalence in the upcoming winter. We found the transmission rate (β') increased as the minimum, mean, maximum temperature rose from -5°C (23°F) and reach the peak at 7°C (44.6°F), 10°C (50°F), and 15°C (59°F), respectively, and then started to decline at higher temperature across the 29 provinces. It is coincident with the curves reported by Wang Mao *et al*[3], who have claimed that the peak of accumulative cases of 492 cities appeared at the minimum, average and maximum temperature of 6.7°C(44.06°F), 8.72°C(47.7°F) and 12.42°C(54.36°F) respectively. The optimal mean temperature ranges for COVID-19 transmission was 5°C-14°C (41°F-57.2°F). Lowen Ac *et.al* proved that influenza virus transmission by droplets was greater and the peak duration of virus shedding lasted longer at 5°C (41°F) than 20°C (68°F)[15]. Indeed, the β' of COVID-19 at 5°C (7.39±1.62) was higher than β' at 20.25°C (4.39±1.63). Another similar infectious disease, SARS was found with higher transmission in temperature<24.6°C than >24.6°C circumstance in Hong Kong [16]. From the curve we illustrated, we could suspect the transmission rate would further reduce at higher temperature over 20.25°C (68.45 °F). It can be expected that COVID-19 pandemic spreading would mitigate for the northern hemispheres in the coming summer, but it is likely to become a seasonal infectious disease. The broader range of air temperature for optimal COVID-19 transmission strongly suggests the necessity and urgency of vaccine at present or in the future.

After first-level public health emergency response on the Jan 23, 2020, integrated NPIs in Mainland China during the epidemic of COVID-19 [2]. The classical SEIR based NPI model usually have to be staged to simulate the propagating stage and NPI stage separately, instead, ScEIQRsh model can well fit the realistic provincial epidemic and NPI data of COVID-19 in China entirely without halfway adjustment of the parameters. The assumption of ScEIQRsh model makes it a model to depict intra-acquaintance spreading pattern, and if Sc were replaced with all the susceptible, it could degenerate into classical SEIR model. That's the reason why ScEIQRsh model can well fit both COVID-19 epidemic and NPI data of China. Because the contact among acquaintances is more frequent than the contact among the whole population, the β' value is usually larger in our intra-acquaintances model than that of classical SEIR model in other studies [17].

According to the ScEIQRsh model, CR and η are more effective to diminish the eventual accumulative number of COVID-19 cases than CCT parameters κ and ρ. In case of insufficiency of medical resources, the better way to improve η could be enlargement of the laboratory capacity for SARS-COV-2 testing or building makeshift hospitals to increase bed capacity [18]. Contact tracing is also helpful for mitigating COVID-19 spreading, which can be regarded as a reminder to be more precautious for close contacts (quarantine for targeted susceptible) than the common susceptible. The surveyQ (κ•ρ) of CCT could be improved with adding more CCT staffs, loosening the criteria of close contacts in CCT, broadening SARS-COV-2 testing to close contacts, or using digital tools. It is undeniable that above methods require more human and financial resources, and may not be suitable for every country in reality. Nevertheless, lockdown and stay-at-home affects the society and economy seriously, contact tracing is an alternative option with less quarantine and consumptions. In brief, keeping the contactable susceptible (Sc or c) in extremely low level and maintaining η in high level are crucial for COVID-19 control.

Additionally, the asymptomatic infectors with contagiousness are source for recurrence of COVID-19 epidemic. We demonstrated that the median and highest proportion of asymptomatic infectors were 14.88% and 34.36% respectively. It was consistent with the reported 18% in 700 infectors never showed symptoms on *Diamond Princess* by Kenji Mizumoto *et al* [19] and claim of 30.8% asymptomatic cases in 565 Japanese citizens evacuated from Wuhan by Hiroshi Nishiura *et al* [20]. The low air temperature could also increase the proportion of asymptomatic infectors. Hence, the implementation of the containment measures is crucial in winter. Clinically significant features of COVID-19 such as incubation and communicable period deducted from ScEIQRsh model are accorded with their observable counterparts, which indicates that the model simulates the transmission process in real-word situation. The calculated median incubation period of COVID-19 was 4.16 days (IQR 3.60, 4.71), which was close to the reported 3 days in a study of including 1,099 laboratory-confirmed cases by Zhong N.S *et al* [21] and 5.1 days in 181 confirmed cases of COVID-19 by Lessler Justin *et al* [22]. The median communicable period ($1/\gamma$) of asymptomatic infectors was computed as 6.77 days (IQR 4.53, 10.36), which was near the 9.6 days in 24 asymptomatic infectors reported by Shen H.B *et.al* [23].

This study only included the epidemic date of Mainland China for model validation because we cannot access the NPIs data, e.g., close contacts of other countries. This model could be fitted even if the NPIs data is sparse, but with less accuracy. The limited latitude spans made the range of air temperature not so broad, especially for higher temperature, though the association of air temperature with COVID-19 transmission rate was informative and suggestive. The proportion of asymptomatic infection was smaller than some other reports, which may due to the meaning of asymptomatic infectors has changed. The asymptomatic infectors mentioned in latter reports usually indicated SARS-COV-2 RNA positive individuals without symptoms, and this could happen in the early infection phase of SARS-COV-2.

Conclusions

In conclusion, we provided a new tool for quantitative assessment the influence of air temperature or prediction of the effectiveness of NPIs strategy on COVID-19 spearing of China, which provided new evidence to decision making of effective public health intervention strategy for COVID-19 prevention and control. This model is also applicable for any other regions because the proportion of acquaintances and strangers could auto-adjust by the fitting process, and it is also suitable for other similar infectious disease.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare no competing interests.

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Contributors

DL and QT are joint first authors, contributed equally to this article for drafting the manuscript. BS and LZ conceived and designed the study. QT, MP and YW collected the epidemiological data of each province in Mainland China. BS and DL analyzed the date with the help of YW and MP. DL and QT drafted the manuscript. BS and LZ revised the manuscript critically. All authors reviewed and approved the final manuscript. LZ (ZHANGLEI_FKYY@163.COM) and BS (subo_group@hotmail.com) are the co-corresponding authors and the guarantors. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Tables

Table 1. The definition and setting range of parameters in ScEIQRsh model

Parameters	Definition	Method	Setting range

Sc	contactable susceptible under the social NPIs	MCMC	[1, 0.01N]
β'	transmission rate, the number of infected people by one infector	MCMC	[1,19]
σ	transition rate from exposure to being contagious	MCMC	[0.27,0.5]
γ	recovery rate of asymptomatic infector	MCMC	[0.04,0.3]
η	hospitalization rate and pace of symptomatic infectors	MCMC	[0.001,0.999]
κ	extent of epidemiological investigations	MCMC	[0,350]
ρ	positive rate of COVID-19 in quarantined people	MCMC	[0,0.1]
ω	transited rate of quarantined people developing to contagious per day	MCMC	[0.07,0.6]
CR	the proportion of contactable susceptible (Sc) under the interventive social prevention	Sc/N	-
Ipd	the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent	1/σ+1/η	-
utI%	the proportion of untraceable infectors, approximately equates to the asymptomatic	γ/(η+κρη+γ).	-
SurveyQ	the quality of contact tracing	κ•ρ	-
Cpd	the time for untraceable infectors with contagious among susceptible	1/γ	-

Abbreviation: Ipd: Incubation period; Cpd: communicable period; utI%: Proportion of asymptomatic infectors; N: the total population of a province. * Details in the supplementary methods

Table 2. The median value of parameters and indexes across 29 provinces of Mainland China by the fitted ScEIQRsh model.

Variables	Median	IQR 25%, 75%	Range
β'	10.22	8.47, 12.35	3.29-15.06
σ	0.42	0.40, 0.44	0.33-0.48
γ	0.15	0.10, 0.22	0.05-0.26
η	0.69	0.47, 0.87	0.16-0.97
κ	42.0	27.83, 60.78	5.35-147.79
ρ (%)	0.9%	0.4%-1.6%	0.03%-5.10%
ω	0.12	0.10, 0.15	0.07-0.21
Sc	26.98	13.97, 54.57	5.91-25525.54
CR	6.84E-07	3.77E-07, 1.44E-06	1.64E-07-4.33E-04
Ipd	4.17	3.60, 4.71	3.27-9.62
utI%	14.88%	8.17%, 25.37%	3.92%-34.36%
SurveyQ	0.39	0.22, 0.55	0.04-2.61
Cpd	6.77	4.53, 10.36	3.91-19.90
1/σ	2.39	2.26, 2.56	2.07-3.01

Abbreviation: Ipd: Incubation period; utI%: Proportion of asymptomatic infectors; Cpd: communicable period

Figure legend

Figure 1. The flow diagram of ScEIQRsh epidemiological model

Six compartments: contactable susceptible (Sc), exposed individuals (E), infected individuals who were outsides of the public health measures (I), close contacts being in quarantine (Q), self-recovery individuals (Rs) and the cumulative hospitalized individuals (Rh). The flow velocities between the compartments are indicated.

Figure 2. The fitting curves of confirmed cases and close contacts predicted by ScEIQRsh model from Day 0-the 23rd, Jan, 2020

A: The fitting curves of confirmed cases and close contacts in Beijing, the representing of North China.

B: The fitting curves of confirmed cases and close contacts in Liaoning, the representing of Northeast China.

C: The fitting curves of confirmed cases and close contacts in Jiangxi, the representing of East China.

D: The fitting curves of confirmed cases and close contacts in Guangdong, the representing of South China.

E: The fitting curves of confirmed cases and close contacts in Gansu, the representing of Northwest China.

F: The fitting curves of confirmed cases and close contacts in Sichuan, the representing of Southwest China.

G: The fitting curves of confirmed cases and close contacts in Hubei, the representing of Central China.

Figure 3. The association between transmission rates (β') of COVID-19 and air temperature of 29 provinces

A, B: A, the transmission rates of COVID-19 among acquaintances for the 29 provinces grouped by geographical regions. B Mapping the transmission rate of COVID-19 in 29 provinces of Mainland China. In figure A and B, the number represents the provinces of each geographical region. North China: 1-5; Northeast China: 6-8; East China: 9-15; Central China: 16-18; South China: 19-21; Northwest China: 22-25; Southwest: 26-29.

C. Mapping the daily mean temperature from the 15th, Jan, 2020 to the 15th, Feb, 2020 in 29 provinces of Mainland China.

D: The association between daily minimum temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

E: The association between daily mean temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

F: The association between daily maximum temperature and the transmission rate, β' of COVID-19 depicted by LOESS. Different color dot represents the temperature of one province.

Figure 4. Evaluation of three NPI measures effectiveness and the suppositional simulation for the measures function

A: The CR calculated by the model in 28 provinces. In B, C, E, F, H, I figure, the solid curves are the fitted curves through our modeling analysis. The meaning of the dash line curves is the suppositional simulation curves after mandatory adjusting three NPI measures' value with different extent. The small dash line means the up-regulation of the NPI measures' value, and the big dash line means the down-regulation of the NPI measures' value. The red curves representing the compartment of Rh; the purple one representing the Q compartment; the orange one representing the I compartment.

B: When we adjusted the CR with 30%-up or down, the change of Rh, Q and I compartments.

C: When adjusted the CR with 50%-up/down, the change of Rh, Q and I compartments.

D: The hospitalization rate and pace, η, of the 29 provinces.

E: The change of Rh, Q and I compartments after adjustment of η with 30% -up/down.

F: The change of Rh, Q and I compartments after adjustment of η with 50% -up/down.

G: The quality of contact tracing, surveyQ was depicted among 29 provinces.

H: The simulation of Rh, Q and I compartments after adjustment of κ for 1/3 down or 3 times up.

I: The simulation of Rh, Q and I compartments after adjustment of ρ- 1/3 down or 3 times up.

Figure 5. The transmission patterns of COVID-19 under social NPIs and the association of untraceable infectors with surveyQ, η and air temperature.

A: A representative example of intra-family and intra-acquaintance transmission pattern of COVID-19 in Beijing.

B: A representative example of COVID-19 transmission pattern among strangers in a large mall.

C: Stranger-stranger transmission is the blind zone of contact tracing.

D: The median proportion of asymptomatic infectors among 29 provinces.

E: The nonlinear association between the ration of untraceable infectors and surveyQ. Higher surveyQ could reduce the ration of untraceable infectors. But as the surveyQ increasing, the proportion of untraceable infectors would be constant.

F: The nonlinear association between the ration of untraceable infectors and η. Higher η could reduce the ration of untraceable infectors either.

G: The relationship between the ration of untraceable infectors and the daily mean temperature.

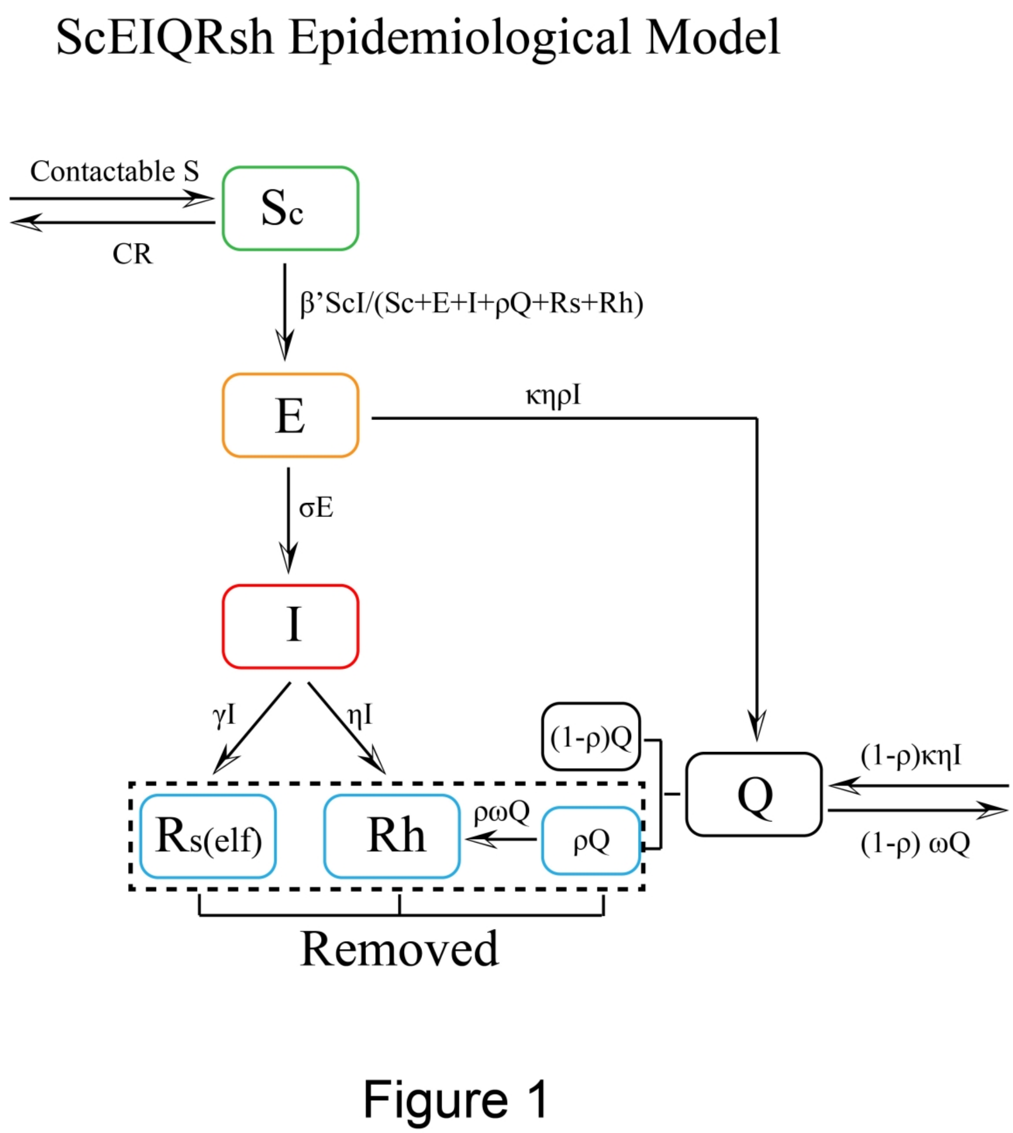

Figure 1

Figure 1

243x274mm (300 x 300 DPI)

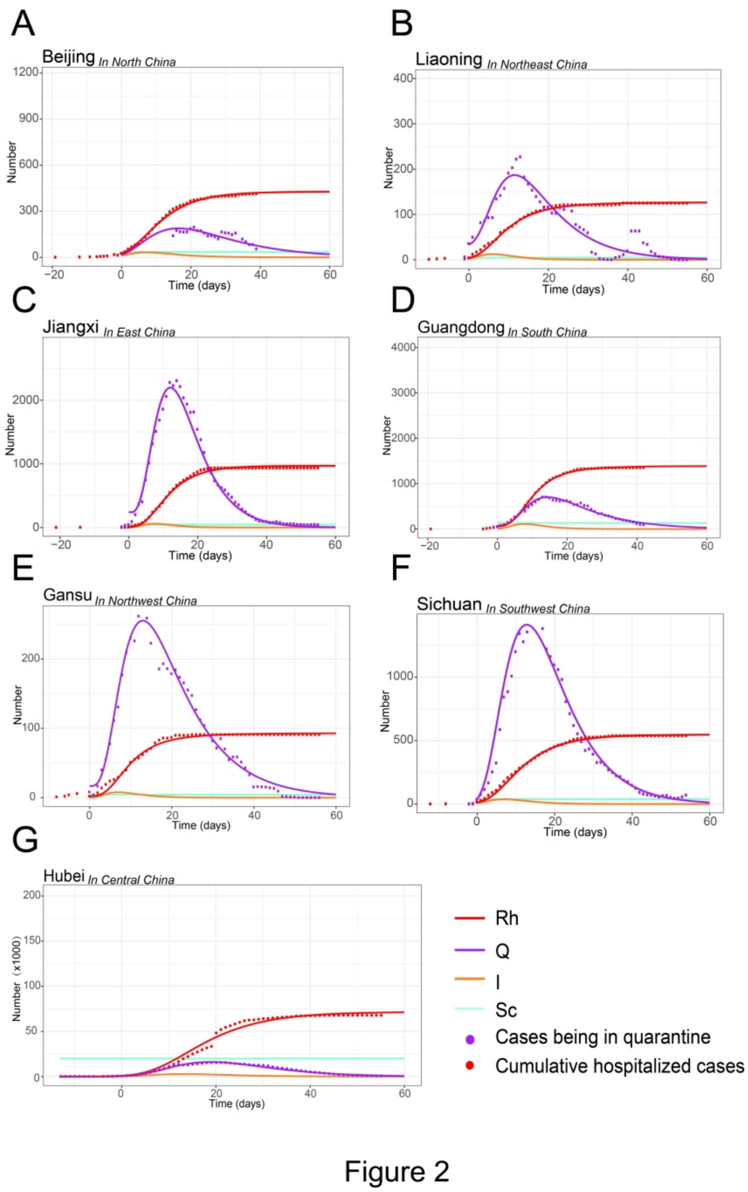

Figure 2

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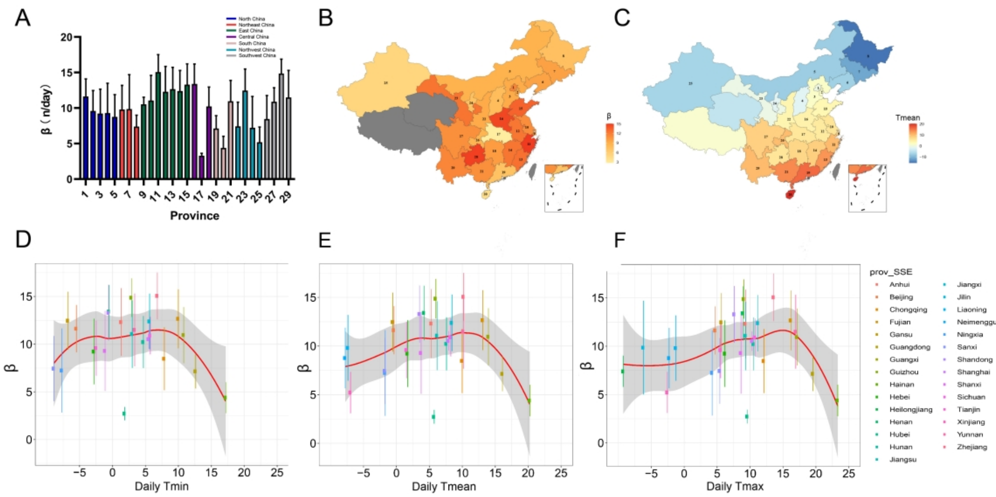

Figure 3

Figure 3

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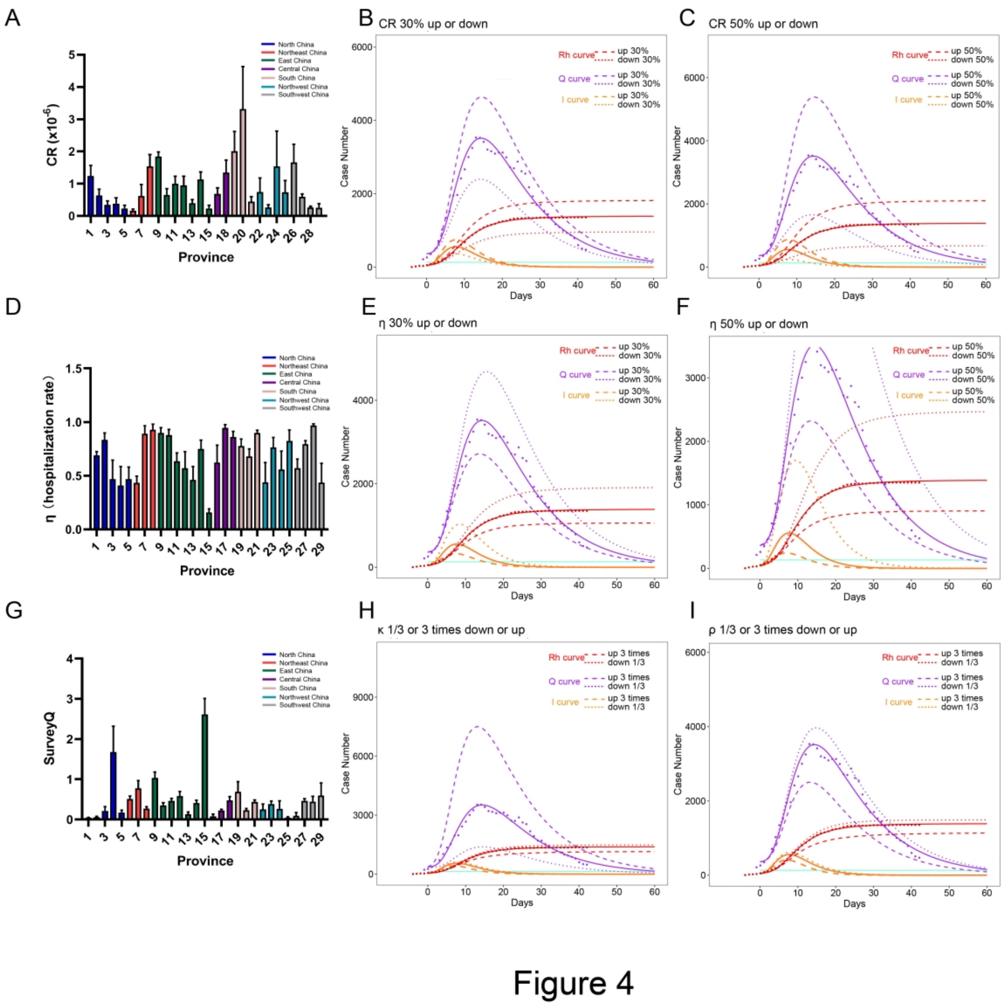

Figure 4

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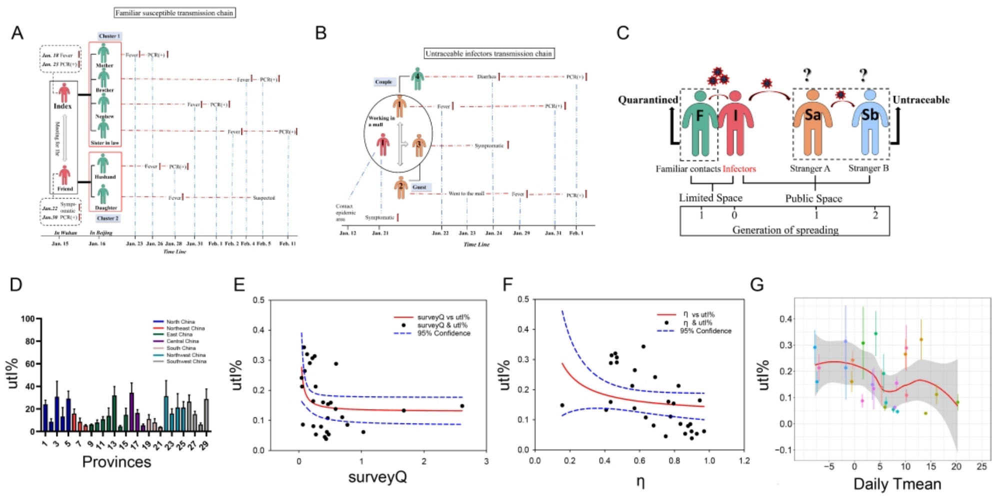

Figure 5

Figure 5

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The impact of air temperature and containment measures on mitigating the intra-household transmission of COVID-19: a novel data-based comprehensive modeling analysis

Di Liu [*,1], Qidong Tai [*,2], Yaping Wang [3], Miao Pu [3], Lei Zhang [†,2], Bo Su [†,1]

Supplementary methods

The stochastic ScEIQRsh epidemiological model

To simulate the epidemiological data of COVID-19 intra-household transmission under NPIs implementation, we developed an early spreading, early non-pharmaceutical-intervention stochastic model, denoted as ScEIQRsh model. The flow diagram of ScEIQRsh model was as the following, which demonstrated as following:

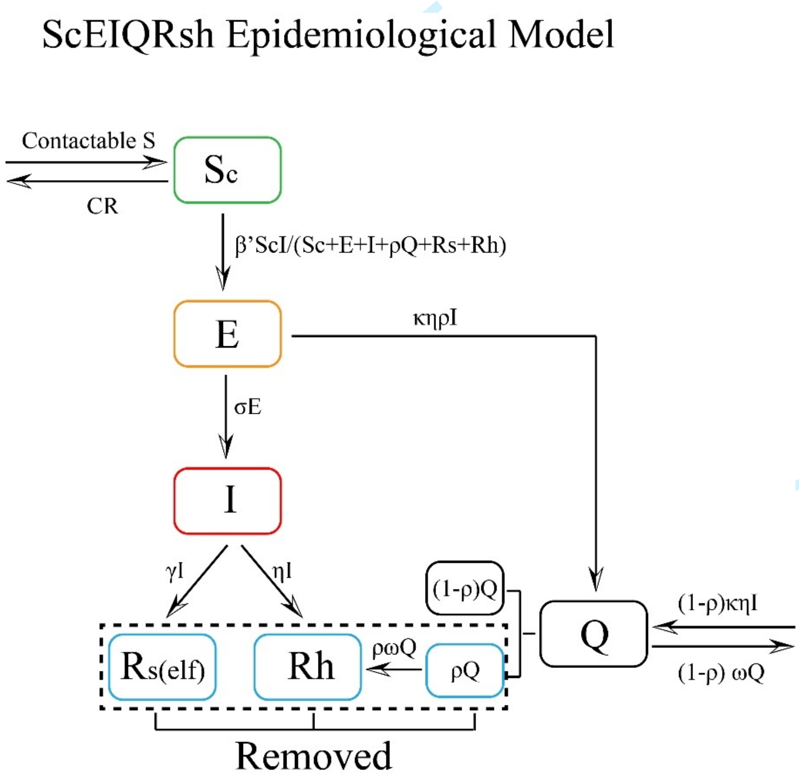

Figure 1

Compartments of the stochastic ScEIQRsh model

Sc: The contactable susceptible subpopulation for the infectors, comprised of their family, relatives, co-workers, friends, and some strangers who could be contacted by the infector under the interventive social prevention. The initial Sc is defined as a continuous random variable with Gaussian distribution in the model. The left arrow of Sc

means the susceptible could be entered into this compartment to become the contactable susceptible (just a part of the susceptible) at the rate of c.

E: The exposed individuals who are in the incubation period after effective contact with the infectors.

I: The infectors, either immigrant or local reproductive infectors who are still outsides of the public health measures.

Q: The close contacts of infectors found out by epidemiological survey, and notified to be in self-quarantine at home, in the hotel or indicated isolating room for 14-day medical observation. The Q value in this model is the daily reported cumulative close contacts or entry of medical observation minus the daily cumulative dismission of medical observation for each province. The right arrow of Q means the quarantined individuals who are not be diagnosed as infectious leave the compartment Q to be the susceptible again at the rate of $(1\text{-}\rho)\ \omega Q$, the opposite arrow means the susceptible in close contacts (in fact, only a small part of close contacts in contact tracing were infected, and the other were still the susceptible) enter the compartment Q at the rate of $(1\text{-}\rho)\kappa\eta I$.

Rs(elf): No all the infectious may see a doctor, especially the non-symptoms infectors. Some of the COVID-19 cases can be self-healing. Thus, the self-recovery individuals who have never be diagnosed and hospitalized because of mild symptoms, or asymptomatic infection, and thus were not be recorded in the daily official epidemic reports is designated as Rs.

Rh: The cumulative individuals who were etiologically diagnosed (mostly SARS-CoV-2 RNA rtPCR positive in oropharyngeal swabs, and inconsistent with other clinical symptoms) and hospitalized in isolate wards. The cumulative number includes any hospitalizing, or dead, or cured COVID-19 patients. In China, every confirmed case had been hospitalized in isolation wards, he/she cannot infect others, so can be regarded as removed.

Removed: The removed means any infectors who have been deprived of the ability to propagate, either by the gain of immunity (Rs, cured in Rh) or by public health measures (infectors in Q, the hospitalizing in Rh), or death (the dead in Rh). The removed in this model is the sum of cumulative Rs, Rh, and the positive cases in Q. So, the flow velocity to Rs and Rh was different.

Parameters of the stochastic ScEIQRsh model

β': the effective transmission rate for the contactable susceptible (Sc).

σ: the progression rate from exposed to being infectious, which is the reciprocal of the incubation period (days) in the propagate chain.

γ: the removal rate for Rself, which is the reciprocal of the apparent period of being propagating for a self-recovery infector in the propagate chain.

η: the removal rate for Rh, which is the reciprocal of the apparent period of being propagating for a hospitalized infector in the propagate chain.

κ: the average number of traceable close contacts for each confirmed case, which was investigated and notified to be in quarantine by the epidemiological survey group of each province. All the found close contacts were assumed to be in a 14-day quarantine.

ρ: the virus-positive rate of the individuals in quarantine for each province.

ω: the dismiss rate of virus-negative individuals in quarantine

Formulation and Parameters setting of ScEIQRsh model

The simultaneous differential equations system for the stochastic ScEIQRsh model is as follows:

(1) $dE/dt = \beta' ScI/(Sc+E+I+Rs+Rh+\rho Q) - \kappa\eta\rho I - \sigma E$

(2) $dI/dt = \sigma E - \eta I - \gamma I$

(3) $dQ/dt = \kappa\eta I - \omega Q$

(4) $dRh/dt = \eta I + \rho\omega Q$

(5) $dRs/dt = \gamma I$

* In equation (1), unlike the classical SIR or SEIR model, the denominator of flow-in velocity is (Sc+E+I+Rs+Rh+ρQ) instead of N or any other constants. The denominator means all the transmitted individuals in the system. The classical SIR or SEIR model assumes that the infectors mix up with different susceptible every day, and ScEIQR model assumes that the infectors mix up with the fixed contactable susceptible every day.

The parameters setting: β', σ, γ and η were set as random variables with Gaussian distribution; κ, ω, ρ was set as random variables with uniform distribution. Parameters range setting: β'[1,19], σ[0.27,0.5], γ[0.04,0.3], η[0.001,0.999], κ[0,350], ω[0.07,0.6], ρ[0,0.1].

Sc was set as a random variable with Gaussian distribution and the range setting was Sc(0,0.002N]. N denotes the total population of the province. The other initial compartment values were estimated as the following: initial Rh=H0, initial Rs=0, initial Q=Q0, initial I=H0*(1-η)/η, initial E= initial I/σ. H0, Q0 denotes the cumulative hospitalized cases, close contacts in quarantine at Day 0 (23rd, Feb 2020) reported by the public health administration of the province. If H0 or Q0 is missing for some province, H0 or Q0 will be given an assumed number.

Model validation

The value of parameters was randomly sampled with one of MCMC method, Metropolis-Hastings (M-H) algorithm, and documented under an appropriate tolerance of best fitting with at least 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for every province of Mainland China.

Other indexes

CR: restriction factor, the proportion of contactable susceptible (Sc) over the total population of a province under the interventive social prevention, which is simply calculated as Sc/N.

utI%: the proportion of the self-recovery removed, including asymptomatic infections or any infection without hospitalization and report, which were estimated as $\gamma/(\eta+\kappa\rho\eta+\gamma)$.

SurveyQ: an estimation for the quality of the epidemical survey, which is calculated as $\kappa \cdot \rho$.

Incubation period: The incubation period was the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent, calculated with $1/\sigma+1/\eta$.

Communicable period: The time for untraceable infectors with contagious among susceptible, calculating with $1/\gamma$.

The air temperature of every province during the COVID-19 outbreak and spreading

The historical meteorological data were collected from china's meteorological administration. The daily mean air temperature was calculated from Jan 15, 2020 to Feb 15, 2020, i.e., from a week before Jan 23, 2020, to 3 weeks after that. In this period, COVID-19 began spreading and controlled by NPI in most of the provinces of China, except Hubei.

The epidemical data and epidemical survey of 31 provinces

The daily confirmed and quarantined cases were used for fitting the model. Almost all the diagnosed cases were hospitalized in isolation wards simultaneously according to the Guidance, thus the reported confirmed cases were just the hospitalized infectors in China. Cases confirmed with a laboratory test of the same sample identified two targets positive detection with real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assay or high-throughput sequencing, one is ORF, another one is the N protein of SARS-CoV-2. The quarantined cases were the population close contact the confirmed cases, asymptomatic infections, and suspected cases identified with epidemiological investigation within 24 hours. The close contacts were including:

1) living, studying, working in the same house with the confirmed or suspected cases.

2) medical staff, family members, or other persons who have close contact with cases in the process of diagnosis, treatment, or nursing.

3) take the same transport and have close contact with infectors, including caregivers, peers, or other passengers(*31*).

The quarantined people were isolated in the home or a specific place for observation of their symptoms for 14 days. If the lab testing results of close contacts of confirmed cases and asymptomatic infections are negative during the medical observation period, they still need to continue quarantine until the end of the observation of 14 days. Those who are in close contact with suspected cases can be relieved of medical observation when suspected cases are excluded from infection.

The provinces of China

There are 34 provincial-level administrative divisions of China, including 23 provinces, 4 municipalities (Beijing, Tianjin, Shanghai, Chongqing), 5 autonomous regions (Guangxi, Inner Mongolia, Tibet, Ningxia, Xinjiang) and 2 special administrative regions (Hong Kong, Macau). 23 provinces are including Anhui, Fujian, Gansu, Guangdong, Guizhou, Hainan, Hebei, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Liaoning, Qinghai, Shaanxi, Shandong, Shanxi, Sichuan, Yunnan, Zhejiang, Taiwan. Seven geographical regions were classified as Mainland China, named as North China, Northeast China, East China, Central China, South China, Northwest China, Southwest China. The 29 provinces were included in our study, and they were separated into each geographical region and represented by numbers as follows:

1) North China: Beijing, Tianjin, Hebei, Shanxi, Inner Mongolia (1-5);

2) Northeast China: Liaoning, Jilin, Heilongjiang (6-8);

3) East China: Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong (9-15) and Taiwan;

4) Central China: Henan, Hubei, and Hunan (16-18);

5) South China: Guangdong, Hainan, Guangxi (19-21), Hongkong, and Macau;

6) Northwest China: Shaanxi, Gansu, Ningxia, Xinjiang (22-25) and Qinghai;

7) Southwest China: Chongqing, Sichuan, Guizhou, Yunnan (26-29), and Tibet.

Supplementary tables

Table S1. The mean value of parameters and indexes in each province of Mainland China

	Parameters and indexes (Mean±SD)										
Province	**β'**	**σ**	**γ**	**η**	**κ**	**ρ(%)**	**ω**	**CR**	**Ipd (day)**	**utI%**	**Survey Q**
All provinces	10.01±2.86	0.42±0.04	0.16±0.07	0.68±0.20	45.55±28.66	1.32±1.30	0.12±0.03	1.58E-05±7.88E-05	4.31±1.18	15.63±9.27	0.46±0.53
Beijing	11.63±2.48	0.35±0.02	0.23±0.05	0.69±0.04	5.59±0.17	0.78±0.12	0.07±0	1.24E-06±3.24E-07	4.34±0.19	24.22±3.57	0.04±0.01
Tianjin	9.58±2.89	0.33±0.03	0.08±0.03	0.83±0.06	12.79±0.72	0.49±0.12	0.07±0	6.35E-07±1.95E-07	3.71±0.3	8.7±2.58	0.06±0.02
Hebei	9.22±3.44	0.41±0.06	0.22±0.06	0.47±0.18	46.56±6.34	0.47±0.24	0.16±0.02	3.38E-07±1.27E-07	5.05±1.07	30.75±13.89	0.22±0.11
Shanxi	9.29±4.2	0.41±0.05	0.14±0.07	0.41±0.18	65.78±15.26	2.49±0.57	0.14±0.02	3.77E-07±1.82E-07	3.89±1.29	13.35±7.9	1.68±0.64
Neimenggu	8.77±3.12	0.44±0.03	0.22±0.04	0.47±0.11	62.99±5.38	0.27±0.08	0.15±0.01	2.34E-07±9.11E-08	4.55±0.59	29.11±6.61	0.17±0.06
Liaoning	9.81±3.38	0.48±0.02	0.13±0.04	0.43±0.06	27.96±1.68	1.82±0.27	0.12±0.01	1.64E-07±5.09E-08	4.46±0.35	15.98±4.01	0.51±0.08
Jilin	9.85±4.85	0.41±0.06	0.15±0.06	0.89±0.07	58.58±14.51	1.35±0.28	0.13±0.03	6.15E-07±3.60E-07	3.6±0.38	8.62±3.27	0.77±0.2
Heilongjiang	7.39±1.62	0.44±0.03	0.07±0.01	0.93±0.05	27.83±1.98	0.98±0.16	0.11±0.01	1.53E-06±3.76E-07	3.35±0.19	5.43±0.73	0.27±0.05

Shanghai	10.53±1.01	0.41±0.07	0.12±0.01	0.9±0.05	64.41±2.25	1.6±0.19	0.21±0.02	1.84E-06±1.44E-07	5.44±0.54	6.22±0.42	1.03±0.15
Jiangsu	11.06±3.55	0.44±0.04	0.1±0.03	0.88±0.05	32.43±3.1	1.08±0.12	0.15±0.01	6.53E-07±1.96E-07	3.45±0.24	8.01±2.27	0.35±0.06
Zhejiang	15.06±2.46	0.48±0.02	0.11±0.03	0.64±0.08	34.64±2.55	1.33±0.16	0.1±0.01	1.00E-06±2.37E-07	3.67±0.24	10.83±2.35	0.46±0.06
Anhui	12.31±3.55	0.38±0.03	0.14±0.07	0.57±0.15	36.65±4.4	1.61±0.29	0.13±0.01	9.51E-07±2.86E-07	4.55±0.55	13.88±7.03	0.59±0.11
Fujian	12.66±3.09	0.45±0.03	0.23±0.04	0.46±0.12	42.01±2.93	0.31±0.14	0.13±0.01	3.89E-07±1.17E-07	4.55±0.61	32.08±7.71	0.13±0.06
Jiangxi	12.38±2.91	0.41±0.03	0.05±0.01	0.75±0.08	48.15±2.52	0.86±0.11	0.16±0.01	1.13E-06±2.36E-07	3.81±0.18	4.59±0.8	0.41±0.07
Shandong	13.3±2.94	0.35±0.06	0.1±0.06	0.16±0.03	51.26±3.2	5.09±0.69	0.08±0.01	2.36E-07±9.04E-08	9.62±1.3	14.88±5.82	2.61±0.4
Henan	13.4±2.8	0.45±0.03	0.26±0.03	0.62±0.16	24.87±2.71	0.31±0.18	0.12±0.01	6.84E-07±1.90E-07	4.56±0.95	34.36±8.6	0.08±0.05
Hubei	3.29±0.34	0.42±0.05	0.23±0.04	0.95±0.03	5.35±0.62	4.28±0.48	0.11±0.01	4.33E-04±8.35E-05	3.48±0.29	16.49±2.9	0.23±0.03
Hunan	10.22±2.73	0.45±0.03	0.07±0.01	0.86±0.05	38.98±2.47	1.22±0.2	0.16±0.01	1.35E-06±3.82E-07	3.42±0.19	5.44±1.2	0.48±0.09
Guangdong	7.14±1.79	0.44±0.04	0.16±0.06	0.78±0.06	14.33±1.33	4.87±1.82	0.17±0.02	2.01E-06±6.07E-07	3.58±0.26	11.14±3.78	0.69±0.25
Hainan	4.39±1.63	0.44±0.04	0.07±0.03	0.68±0.07	23.03±1.83	1±0.18	0.08±0.01	3.32E-06±1.31E-06	3.78±0.25	8.17±3.17	0.23±0.05
Guangxi	10.95±2.94	0.46±0.02	0.05±0	0.9±0.03	52.88±2.53	0.82±0.08	0.11±0	4.45E-07±1.51E-07	3.27±0.13	3.92±0.3	0.43±0.05
Shaanxi	7.44±3.41	0.4±0.05	0.22±0.05	0.44±0.18	76.13±8.4	0.33±0.17	0.1±0.01	7.43E-07±4.38E-07	5.52±1.91	31.44±13.72	0.25±0.13
Gansu	12.46±3.04	0.45±0.03	0.2±0.05	0.76±0.09	41.99±3.6	0.92±0.14	0.1±0.01	2.66E-07±7.72E-08	3.56±0.27	16.08±4.02	0.39±0.07
Ningxia	7.24±4.41	0.36±0.06	0.17±0.07	0.56±0.17	70.9±11.44	0.37±0.26	0.11±0.02	1.53E-06±1.10E-06	4.91±1.29	21.31±12.15	0.27±0.19
Xinjiang	5.21±2.13	0.41±0.05	0.23±0.05	0.82±0.1	147.79±11.06	0.03±0.01	0.08±0	7.34E-07±3.67E-07	3.71±0.32	21.32±5.08	0.05±0.02
Chongqing	8.47±3.31	0.42±0.03	0.22±0.04	0.57±0.08	39.36±6.01	0.22±0.16	0.13±0.01	1.66E-06±5.67E-07	4.17±0.34	26.52±5.82	0.09±0.08
Sichuan	10.9±1.96	0.38±0.03	0.21±0.04	0.79±0.03	46.84±3.25	0.99±0.07	0.12±0.01	5.92E-07±9.07E-08	3.89±0.22	15.47±2.48	0.47±0.05
Guizhou	14.87±2.03	0.35±0.03	0.09±0.02	0.97±0.02	23.7±3.5	1.86±0.37	0.17±0.02	2.63E-07±3.44E-08	3.92±0.25	6.25±1.45	0.45±0.13
Yunnan	11.49±3.82	0.44±0.04	0.25±0.04	0.44±0.18	97.33±33.65	0.59±0.19	0.15±0.04	2.60E-07±1.18E-07	5.14±1.62	28.89±8.82	0.59±0.31

Abbreviation: Ipd: Incubation period; utI%: Proportion of Untraceable infectors;

Supplementary figures and legend

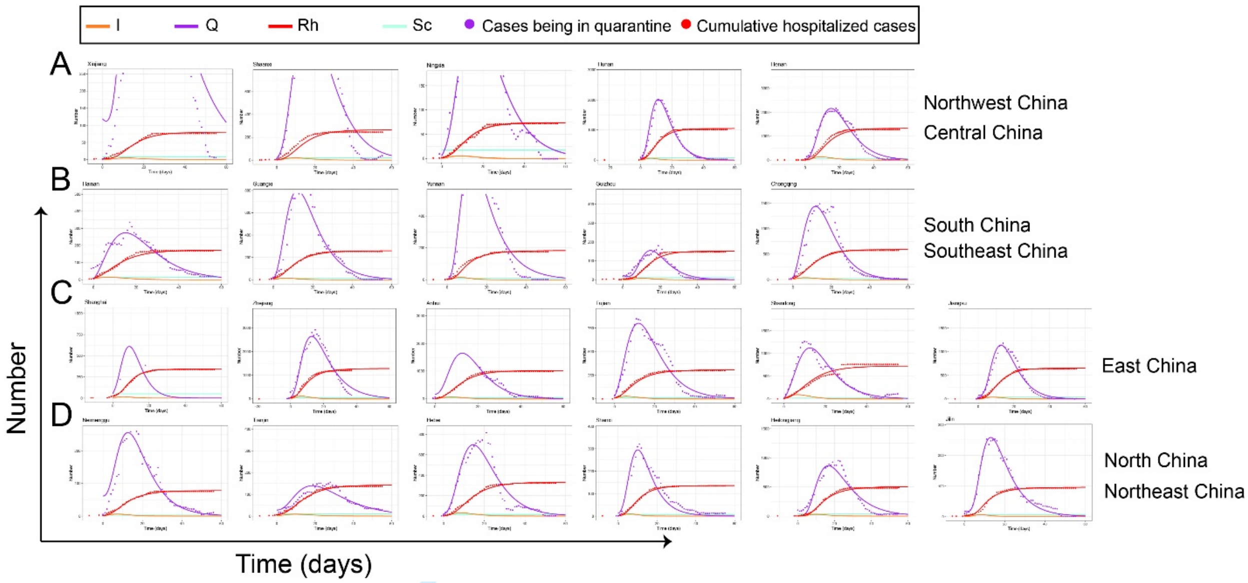

Figure S1. The fitting curves of both the number of daily cumulative confirmed cases and close contacts being in quarantine in 22 provinces of Mainland China (Day 0, the 23rd, Jan, 2020).

A: The fitting curve of provinces in Northwest China- Xinjiang/ Shaanxi/ Ningxia and Central China-Hunan/ Henan.

B: The fitting curve of provinces in South China- Hainan/ Guangxi, and Southwest China-Yunnan/ Guizhou/ Chongqing.

C: The fitting curve of provinces in East China- Shanghai/ Zhejiang/ Anhui/ Fujian/ Shandong/ Jiangsu.

D: The fitting curve of provinces in North China- Neimenggu/ Tianjin/ Hebei/ Shanxi and Northeast China-Heilongjiang/ Jilin.

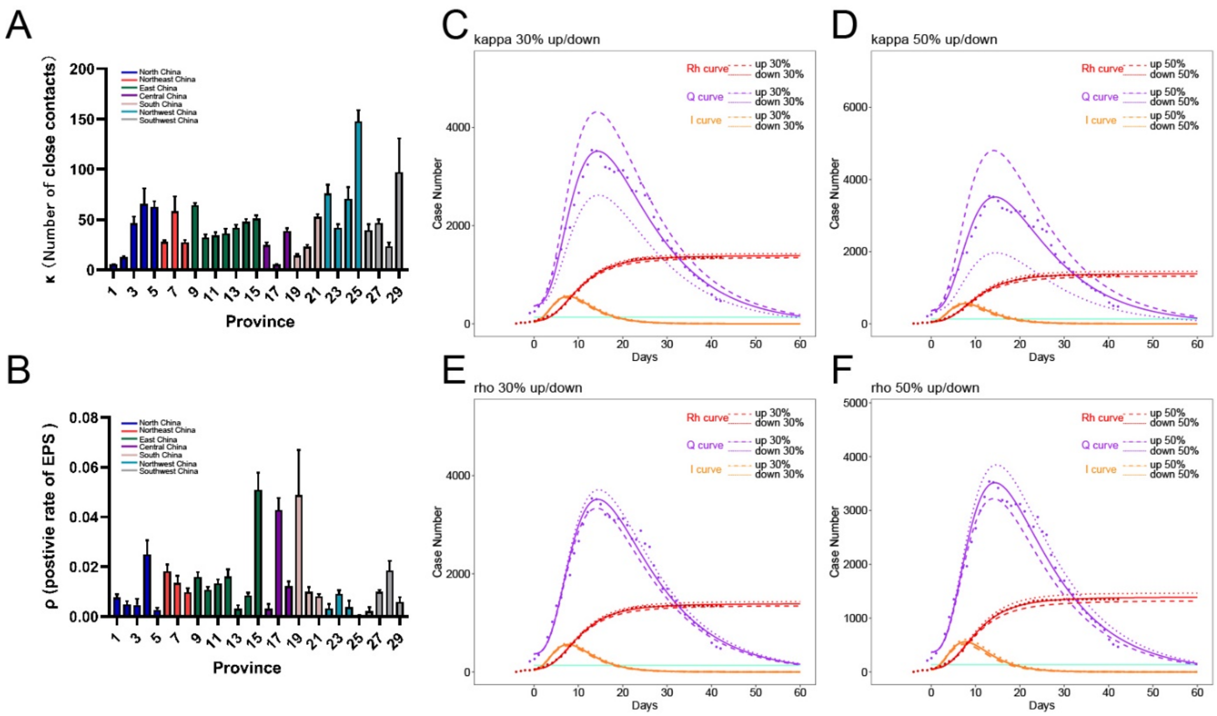

Figure S2. Suppositional simulation of contact tracing parameters, κ and ρ.

A-B: The median κ and ρ was observed as different among 29 provinces.

C-D: The influence on Rh, Q and I compartment after adjustment of κ by 30% or 50%.

E-F: The simulated Rh, Q and I compartment after adjustment of ρ by 30% or 50%.

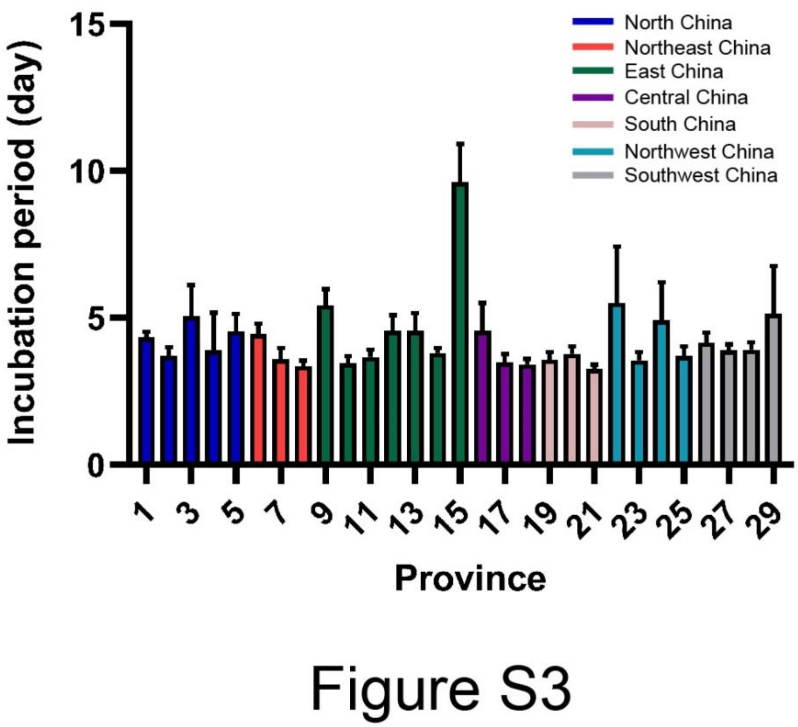

Figure S3. The median incubation period of COVID-19 among 29 provinces.

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The impact of air temperature and containment measures on mitigating the intra-household transmission of COVID-19: a novel data-based comprehensive modeling analysis

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Running Head: Air temperature impacting COVID-19 control

Keywords: COVID-19; air temperature; non-pharmaceutical Interventions; mathematical model; asymptomatic

Abstract

Objectives

Because of the implementation of non-pharmaceutical interventions (NPIs), the transmission pattern of COVID-19 was changed to intra-household spreading. As the second wave of the COVID-19 pandemic worldwide, it was necessarily to re-estimate the influence of temperature on COVID-19 transmission, especially on intra-household transmission.

Methods

We established a stochastic epidemiological model (susceptible-Exposed-Infected-Quarantined-Removed model (ScEIQRsh)) to evaluate the influence of air temperature on COVID-19 transmission and simultaneously to assess the NPIs' effectiveness on containing the intra-household spreading of COVID-19. The model was fitted by Metropolis-Hastings (M-H) algorithm, one Markov Chain Monte Carlo (MCMC) method with a cost function based on least squares method.

Results

This study provides a ScEIQRsh model to assess the influence of air temperature and containment measures on COVID-19 transmissibility. We found that the COVID-19 transmission was influenced by air temperature, which showed the optimal temperature range of 5℃-14℃ (41°F-57.2°F) and peak of 10℃ (50°F) for COVID-19 spreading. From fitted model, the fitted intra-household transmission rate (β') of COVID-19 was 10.22 (IQR 8.47, 12.35) across Mainland China. The association between air temperature and the β' of COVID-19 suggests that COVID-19 pandemic might be seasonal. The effectiveness of NPIs was also validated by our model, which demonstrated that the measures to diminish contactable susceptible (Sc), and to avoid delay of diagnosis and hospitalized isolation (η) were more effective than contact tracing (κ, ρ). But the most effectual way for ultimate COVID-19 control is vaccination.

Conclusions

We constructed a novel epidemic model to estimate the impact of air temperature on COVDI-19 transmission beside the NPIs' implementation, which can be helpful for decision making of

public health strategy, and prediction of the COVID-19 transmission or other infectious disease in the future.

Strengths and limitations of this study

This study provided one novel epidemiological model to mimic the intra-household transmission of COVID-19 and fitted with the epidemic data in China Mainland.

This study investigated the relationship between air temperature and the intra-household transmission rate of COVID-19 besides the influence of non-pharmaceutical interventions (NPI).

The efficiency of NPIs, especially the effect of contact tracing in mitigating the transmission of COVID-19 was studied.

This study only included the epidemic date of Mainland China for model validation because we cannot access the NPIs data, e.g., close contacts of other countries.

This model could be fitted even if the NPIs data is sparse, but with less accuracy.

Introduction

The COVID-19 has been spread for more than one year in many countries. There are many factors, such as the virus virulence, the host defense potential, the number of contacts *et al* that could impact the transmission[1]. Among them, the air temperature might be one important factor for impacting the transmission of SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2), which cause the COVID-19 epidemic, since the influenza virus was affected by the changes of temperature and relative humidity[2]. However, the meteorological indicators impact on COVID-19 transmission is unclear. A few studies reported the air temperature influence COVID-19 pandemic. Bilal and the colleagues found the temperature was significant associated with the COVID-19 pandemic in USA[3 4] and Germany[5] as well. But some researchers published the adverse conclusion[6 7]. It is controversial for the impact of air temperature on COVID-19 transmission.

In the past year, many countries' government implemented non-pharmaceutical interventions (NPIs), including physical and social distancing, quarantine, and isolation to impede the COVID-19 outbreak in the early stage[8]. In China, the pandemic of COVID-19 was prevented within two months under those NPIs executed since Jan 23, 2020. Besides the announcement of keeping physical and social distance to the public, epidemiological survey (EPS) -based quarantine and hospitalized isolation were applied [9]. These containment measures were effective for controlling the spreading of COVID-19. But, what's the influence of temperature on the COVID-19 incidence and transmission besides the NPIs' effect?

We then used the data from China as an appropriate example to evaluate the relationship between the air temperature and COVID-19 spreading. Firstly, the social intervention in China is almost taken at the same time and is almost uniform with different intensity between provinces. Secondary, the latitude span of mainland China is large enough to reflect the zones with daily mean air temperature of -7℃ to 20℃ in winter. At last, we could get the completely data of the daily numbers of cases in quarantine by contact tracing for each province. Thus, we constructed a new kind of SEIR (Susceptible-Exposed-Infected-Removed)-based model, named ScEIQRsh (Contactable Susceptible-Exposed-Infected-Quarantined-Removed) to depict a new spreading pattern of COVID-19, the intra-household transmission. Which can separate the influence of social intervention measures from confounding factors, and with machine learning methods we achieved the precise influence of air temperature on COVID-19 spreading. Also, the effectiveness of the NPIs on control the COVID-19 transmission was validated by this model as well.

Materials and Methods

Development of the dynamical non-classical SEIR model for COVID-19

The developed ScEIQRsh model is an expanded model from classic SEIR epidemic model, which contains six compartments named as Sc (contactable susceptible), E (the exposed to SARS-COV-2), Q (daily close contacts being in quarantine), I (infectors outside of the healthcare system), Rh (accumulative hospitalized infectors), and Rs (self-recovery individuals with asymptomatic infection or mild symptoms who have never be hospitalized and registered in healthcare system) (Figure 1). Sc represents the contactable susceptible under the social NPIs, such as lockdown, social distancing, cancelling gatherings, closing public places, which is set as a random variable in the model. Q reflects the contact tracing (CCT) for quarantine, and Rh reflects the confirmed and hospitalized infectors in isolation wards, and this kind of population was daily reported by public health agency. E, I, and Rs compartments were outside of the healthcare system. Rh is really the reported cumulative confirmed cases in the model. Every compartment has been linked by a few parameters, and the flow velocity of each compartment is illustrated in figure 1 (details in the supplementary methods).

Parameters of the stochastic ScEIQRsh model

The definition and initial range of model parameters of β', σ, γ, κ, ρ, ω, η and Sc in the model were listed in Table 1. β' was the intra-household transmission rate dependent of the property of SARS-COV-2. σ and γ were associated with the intrinsic incubation period and communicable period of COVID-19. κ, ρ and ω were associated with contact tracing and quarantine. η reflected the pace of confirmed diagnosis and hospitalized isolation for infectors. Other indexes could be calculated from the solved model, such as the contact rate (CR), the quality of CCT (surveyQ), the proportion of untraceable infectors (approximately equate to the asymptomatic) (utI%), the incubation period and communicable period of SARS-COV-2, and among them, CR reflects the proportion of Sc in population under the integrated NPIs, surveyQ represents the quality of contact tracing.

β': the effective intra-household transmission rate for the contactable susceptible (Sc).

σ: the progression rate from exposed to being infectious, which is the reciprocal of the incubation period (days) in the propagate chain.

γ: the removal rate for Rself, which is the reciprocal of the apparent period of being propagating for a self-recovery infector in the propagate chain.

η: the removal rate for Rh, which is the reciprocal of the apparent period of being propagating for a hospitalized infector in the propagate chain.

κ: the average number of traceable close contacts for each confirmed case, which was investigated and notified to be in quarantine by the epidemiological survey group of each province. All the found close contacts were assumed to be in a 14-day quarantine.

ρ: the virus-positive rate of the individuals in quarantine for each province.

ω: the dismiss rate of virus-negative individuals in quarantine

Formulation and Parameters setting of ScEIQRsh model

The simultaneous differential equations system for the stochastic ScEIQRsh model is as follows:

(1) $dE/dt = \beta' Sc I/(Sc+E+I+Rs+Rh+\rho Q) - \kappa\eta\rho I - \sigma E$;

(2) $dI/dt = \sigma E - \eta I - \gamma I$;

(3) $dQ/dt = \kappa\eta I - \omega Q$;

(4) $dRh/dt = \eta I + \rho\omega Q$;

(5) $dRs/dt = \gamma I$;

* In equation (1), unlike the classical SIR or SEIR model, the denominator of flow-in velocity is ($Sc+E+I+Rs+Rh+\rho Q$) instead of N or any other constants. The denominator means all the transmitted individuals in the system. The classical SIR or SEIR model assumes that the infectors mix up with different susceptible every day, and ScEIQR model assumes that the infectors mix up with the fixed contactable susceptible every day.

The parameters setting: β', σ, γ and η were set as random variables with Gaussian distribution; κ, ω, ρ was set as random variables with uniform distribution. Parameters range setting: β' [1,19], σ [0.27,0.5], γ [0.04,0.3], η [0.001,0.999], κ [0,350], ω [0.07,0.6], ρ [0,0.1].

Sc was set as a random variable with Gaussian distribution and the range setting was Sc(0,0.002N]. N denotes the total population of the province. The other initial compartment values were estimated as the following: initial Rh=H0, initial Rs=0, initial Q=Q0, initial $I=H0*(1-\eta)/\eta$, initial E= initial I/σ. H0, Q0 denotes the cumulative hospitalized cases, close contacts in quarantine at Day 0 (23rd, Feb 2020) reported by the public health administration of the province. If H0 or Q0 is missing for some province, H0 or Q0 will be given an assumed number.

Acquisition the epidemic data

The intra-household and intra-household transmission of COVID-19 [10] could be observed at the beginning of COVID-19 spreading in Mainland China [11]. And each Provincial Health Commission would report the daily number of close contacts being in quarantine besides reporting the number of daily confirmed cases of COVID-19. This completed data of Mainland China was good for fitting the ScEIQRsh model and investigating the intra-household or intra-acquaintances transmission of COVID-19. We collected the data of daily accumulative confirmed cases of COVID-19 from January to March, 2020 through the 31 Provincial Health Commission of Mainland China. The daily number of close contacts in quarantine and the daily number of whom were relieved of quarantine were also collected from the provincial government website in China. Xizang and Qinghai province were excluded because of few cases, with only one and 18 confirmed cases, respectively. Almost all the diagnosed cases were hospitalized in isolation wards simultaneously according the Guidance, thus the reported confirmed cases were just the hospitalized infectors in China. Details of the criteria of confirmed cases and close contacts in quarantine were clarified in the supplementary methods.

Simulation and model fitting

We fitted both the reported accumulative confirmed cases and daily close contacts in quarantine with Rh and Q compartments by ScEIQRsh model for each province by Markov Chain Monte Carlo (MCMC) method with a cost function based on least squares method. Briefly, model parameters and Sc were random samplings with Metropolis-Hastings (M-H) algorithm, one of Markov Chain Monte Carlo (MCMC) method. The proposal distribution for accept-reject is a Bernoulli distribution from the comparison of the cost function of curve fitting in iteration (better or not). Both simulated curves of Rh and Q were simultaneously fitted with the raw data (the real word data) by the least-squares method. And the cost function was SSE/SST (Sum of Squares for Error/Sum of Squares for Total). The optimized parameters were documented with 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for 29 provinces of Mainland China. The expected value and standard deviation for each parameter were then confirmed.

Air temperature of provinces in China during the COVID-19 spreading

The minimum (Tmin), mean (Tmean), maximum (Tmax) air temperature of each province was collected from the National Meteorological Administration from Jan 15, 2020 to Feb 15, 2020 (one week before and three weeks later of Jan 23, 2020 (Day 0)). The LOESS regression was used to depict the relationship between the air temperature of 29 provinces and COVID-19 transmission rate in ScEIQRsh model.

Patient and Public Involvement

No patient involved

Statistical analysis

The enrolled 29 provinces for model validation were separated into seven geographical regions, named as North, Northeast, East, Central, Northwest, South and Southwest China. The curves of Rh and Q were simultaneously fitted with the raw data by least squares method with tolerance of 1.05. SSE/SST (Sum of Squares for Error/Sum of Squares for Total) as the cost function was . The data process was performed on R (version 3.6.1), and the "deSolve" R package was used as the solver of differential equations. The R source code can be found in *GitHub*. The parameters were denoted as mean±SD for each province, and the median (interquartile range, IQR: 25%, 75%) was used for describing across provinces.

Results

The influence of air temperature on the transmissibility of COVID-19

The intra-household transmission rate (β') was calculated first, and then the nonlinear association between β' and air temperature was depicted by LOESS fitting.

The intra-household transmission rate (β') calculated

Firstly, we fit the COVID-19 transmission with integrated social NPIs by the ScEIQRsh model, which can be well fitted with both the reported number of daily accumulative confirmed cases and close contacts being in quarantine in 29 provinces of Mainland China (Figure 2, Figure S1). The predicted daily Rh and Q compartments were coincident with the provincial reported numbers. From the fitting curves, we obtained the median intra-household transmission rate (β') for 29 provinces were 10.22 (IQR 8.47, 12.35), which implied about 10.22 person would be infected by one infector in case that the susceptible are mostly acquaintances and Sc is extrapolated to infinite (Figure 3A-B, Table 2, Table S1).

The rang of air temperature for COVID-19 spreading

The span of mean air temperature for every province in China was from -15 °C (5 °F) to 20.25 °C (68.45 °F) during the COVID-19 spreading period of Jan to Feb 2020 in China (Figure 3C). The relationship between the air temperature and β' was evaluated. As the daily air temperature increased from subzero (0°C, 32°F), the value of β' raised gradually until the air temperature went up to a peak of 7°C (44.6°F) for minimum daily temperature, 10°C (50°F) for mean or 15°C (59°F) for maximum daily temperature, respectively (Figure 3D, E, F), and then declined sharply as the temperature continued to raise. We observed transmission rate (β') was higher than 11 in the range of 5℃-14℃ (41°F-57.2°F) for mean air temperature, which may be most suitable for COVID-19 spreading.

Validation the NPIs on mitigating the COVID-19 spreading

The second wave of COVID-19 pandemic is appearing in many countries currently because of the coronavirus mutation. But the containment measures are still pivotal for controlling COVID-19 spreading.

Assessment of NPI measures by suppositional simulation

We mainly assessed three independent parameters, contact rate (CR), η and surveyQ, which were crucial for stopping the spreading chain. Based on our model, the median Sc was estimated as 26.98 (IQR:13.97, 54.57) with the highest in Hubei and lowest in Neimenggu province (Table S1). The median CR for 29 provinces was accordingly 6.84E-07 (IQR 3.77E-07, 1.44E-06) (Figure 4A). To illustrate the influence of NPI measures on COVID-19 transmission for ScEIQRsh model, we arbitrarily adjusted CR, κ, ρ, and η value with representative 30% or 50% up/down-regulation to simulate the suppositional spreading situation. If CR were 30% or 50% enlarged, the eventual accumulative hospitalized cases (Rh) would strongly increase, the peak of infectors (I) would be brought backward and vice versa (Figure 4B, 4C). The median for velocity of hospitalized isolation for infectors (η) was 0.69 (IQR 0.47, 0.87) among 29 provinces (Figure 4D). The influence of η is the opposite to CR. If the η were increased as 30% or 50%, the eventual Rh would be strongly reduced and vice versa (Figure 4E, 4F).

SurveyQ, the product of κ times ρ, was 0.39 (IQR 0.22, 0.55), which indicated that 0.39 positive cases were found in close contacts of CCT averagely for each confirmed infector (Figure 4G). The κ and ρ can be used to assess the effectiveness of CCT, and the median κ of 29 provinces was 42.0 (IQR 27.83, 60.78), suggesting that 42 close contacts of one infector had been excavated averagely by CCT groups (Figure S2A). The COVID-19 positive rate (ρ) in close contacts was speculated as 0.98% (IQR 0.47%-1.60%), ranged from 0.03%-5.10% (Figure S2B), which was quite close to the WHO-China joint report of 0.9%-5% in China [11]. In case of enlarged κ or ρ, the eventual accumulative number of confirmed COVID-19 would diminish and the plateau of Rh would be brought forward (Figure 4H, 4I, Figure S2C, D, E, F). On the same adjusted amount, the effectiveness of CR and η on spreading prevention were stronger than that of CCT parameters, κ and ρ. The incubation period and communicable period of COVID-19 was calculated by ScEIQRsh model, and the results were consistency with other studies (Table 2, Figure S3), which reflected the reasonable of this novel model.

Blind zone of contact tracing and asymptomatic infectors in NPIs strategy

With the integrated social NPIs, COVID-19 transmission mostly occurred between free infectors and acquaintances, as well as a few strangers whom the infectors have to contact for daily necessities. In a typical intra-householdintra-acquaintance transmission, the index case transmitted to four of his family members and one friend directly, and the friend's family indirectly infected within half a month[12] (Figure 5A). CCT can easily find close contacts of acquaintances, but be inefficient in finding transmission among strangers in public space. For example, a salesman index transmitted to two unacquainted salesmen in other sales areas sequentially without gathering in a large mall, and a customer without any inquiry and purchase was infected by one of the transmitted salesmen after 30-minutes lingering (Figure 5B). This transmission chain in strangers could not be easily found by contact tracing, and was only revealed after all the participants appeared symptoms (Figure 5C).

Another blind spot of contact tracing is about asymptomatic infection. The calculated proportion of asymptomatic and mild-symptom infectors without hospitalization (the proportion of untraceable infectors, utI%) by ScEIQRsh model was 14.88% (IQR 8.17%, 25.37%), ranged from 3.92%-34.36% across 29 provinces, which implied that average 14.88% COVID-19 patients couldn't be found out with social NPIs, and the average proportion of asymptomatic in COVID-19 patients should be smaller than 14.88% (IQR 8.17%, 25.37%) (Figure 5D). The higher surveyQ of CCT can only reduce but not eliminate utI% (Figure 5E), but high η could decline the utI% constantly (Figure 5F). Hence, contact tracing is not sufficient to find all the infectors, especially in stranger-stranger transmission and asymptomatic infection. The ratio of asymptomatic infectors also influenced by air temperature. When the mean air temperature is subzero, the utI% is high (Figure 5G).

Discussion

Whether the meteorological conditions affect the spread of COVID-19 is vitally important in prediction of COVID-19 prevalence, especially for intra-household transmission in the future. In our study, we found the transmission rate (β') increased as the minimum, mean, maximum temperature rose from -5°C (23°F) and reach the peak at 7°C (44.6°F), 10°C (50°F), and 15°C (59°F), respectively, and then started to decline at higher temperature across the 29 provinces in China. It is coincident with the curves reported by Wang Mao *et al*[13], who have claimed that the peak of accumulative cases of 492 cities appeared at the minimum, average and maximum temperature of 6.7°C(44.06°F), 8.72°C(47.7°F) and 12.42°C(54.36°F) respectively. Wang Mao *et al* [13] and Sajadi MM *et al* [14] found that regions in 30-50º N' corridor with 5°C-11°C (41°F-51.8°F) average temperature had increased COVID-19 transmission. We also coincidentally discovered the optimal mean temperature ranges for COVID-19 transmission were 5°C-14°C (41°F-57.2°F). Lowen Ac *et.al* proved that influenza virus transmission by droplets was greater and the peak duration of virus shedding lasted longer at 5°C (41°F) than 20°C (68°F)[15]. Indeed, the β' of COVID-19 at 5°C (7.39±1.62) was higher than β' at 20.25°C (4.39±1.63). Another similar infectious disease, SARS was found with higher transmission in temperature<24.6°C than >24.6°C circumstance in Hong Kong [16]. From the curve we illustrated, we could suspect the transmission rate would further reduce at higher temperature over 20.25°C (68.45 °F), but not eliminate. It can be expected that COVID-19 pandemic spreading would mitigate for the northern hemispheres in the summer, and it is likely to become a seasonal infectious disease from the currently situation. The broader range of air temperature for optimal COVID-19 transmission strongly suggests the necessity and urgency of vaccine at present.

Besides the influence of air temperature, the most important measures to contain the COVID-19 epidemic is the vaccine and the NPIs. After first-level public health emergency response on the Jan 23, 2020, integrated NPIs were implemented in Mainland China during the epidemic of COVID-19 [9]. The spreading pattern of COVID-19 was changed into intra-household transmission. A report of the "WHO-China Joint Mission on COVID-19" verified in Guangdong and Sichuan province, about 78%-85% of intra-household infections were within families [11]. And in Beijing, there are 176 intra-household cases among 262 confirmed cases and 133 (50.8%) were intra-household cases [10]. We estimate the effectiveness of integrated NPIs to simulate COVID-19 restricted spreading among acquaintances for the first time by our ScEIQRsh epidemic model. ScEIQRsh model can well fit the realistic provincial epidemic and NPI data of COVID-19 in China entirely without halfway adjustment of the parameters. Because, unlike the classical SEIR (Susceptible-Exposed-Infected-Removed) epidemic model assumes that infectors mix up with all the susceptible per day, the infectors of ScEIQRsh mix up with the contactable susceptible per day, which indicates the family members, relatives, co-workers, friends and some contactable strangers for obtaining daily necessities of the infectors. Because the contact among acquaintances is more frequent than the contact among the whole population, the β' value is usually larger in our model than that of classical SEIR model in other studies [17].

In those NPIs measures, CR and η are more effective to diminish the eventual accumulative number of COVID-19 cases than CCT parameters κ and ρ. In case of insufficiency of medical resources, the better way to improve η could be enlargement of the laboratory capacity for SARS-COV-2 testing or building makeshift hospitals to increase bed capacity [18]. Contact tracing is also helpful for mitigating COVID-19 spreading, which can be regarded as a reminder to be more precautious for close contacts (quarantine for targeted susceptible) than the common susceptible. The surveyQ (κ•ρ) of CCT could be improved with adding more CCT staffs, loosening the criteria of close contacts in CCT, broadening SARS-COV-2 testing to close contacts, or using digital tools. It is undeniable that above methods require more human and financial resources, and may not be suitable for every country in reality. Nevertheless, lockdown and stay-at-home affects the society and economy seriously, contact tracing is an alternative option with less quarantine and consumptions. In brief, keeping the contactable susceptible (Sc or c) in extremely low level and maintaining η in high level are crucial for COVID-19 control.

Additionally, the asymptomatic infectors with contagiousness are source for recurrence of COVID-19 epidemic. We demonstrated that the median and highest proportion of asymptomatic infectors were 14.88% and 34.36% respectively. It was consistent with the reported 18% in 700 infectors never showed symptoms on *Diamond Princess* by Kenji Mizumoto *et al* [19] and claim of 30.8% asymptomatic cases in 565 Japanese citizens evacuated from Wuhan by Hiroshi Nishiura *et al* [20]. The low air temperature could also increase the proportion of asymptomatic infectors. Hence, the implementation of the containment measures is crucial besides the air temperature influence. Clinically significant features of COVID-19 such as incubation period deducted from ScEIQRsh model are accorded with the reported 3 days in a study of including 1,099 laboratory-confirmed cases by Zhong N.S *et al*[21], which indicates that the model simulates the transmission process in real-word situation.

Our study based on a novel ScEIQRsh NPIs model, and only included the epidemic date of Mainland China for model validation because we cannot access the NPIs data, e.g., close contacts of other countries. This model could be fitted even if the NPIs data is sparse, but with less accuracy. The limited latitude spans made the range of air temperature not so broad, especially for higher temperature, though the association of air temperature with COVID-19 transmission rate was informative and suggestive[22].

Conclusions

In conclusion, we provided a new tool for quantitative assessing the influence of air temperature or the effectiveness of NPIs strategy on COVID-19 outbreak. We also speculated the appropriate temperature for SARS-COV-2 transmission might be within 5℃-14℃ (41°F-57.2°F) under the implementation of NPIs. The stochastic ScEIQRsh model which can well fit both the early spreading and early social intervention data of COVID-19 was constructed. The effectiveness of NPIs for mitigating the transmission of COVID-19 were evaluated. Keeping the contactable susceptible in low level and promoting the diagnosis and hospitalized isolation of COVID-19 promptly are crucial for mitigating early intra-household transmission of COVID-19, which provided new evidence to decision making of effective public health intervention strategy for COVID-19 prevention. This model is also applicable for any other regions because the proportion of acquaintances and strangers could auto-adjust by the fitting process, and it is also suitable for other similar infectious disease.

Ethics statement

This study does not involve human participants. This study does not involve animal subjects.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare no competing interests.

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Contributors

DL and QT are joint first authors, contributed equally to this article for drafting the manuscript. BS and LZ conceived and designed the study. QT, MP and YW collected the epidemiological data of each province in Mainland China. BS and DL analyzed the date with the help of YW and MP. DL and QT drafted the manuscript. BS and LZ revised the manuscript critically. All authors reviewed and approved the final manuscript. LZ (ZHANGLEI_FKYY@163.COM) and BS (subo_group@hotmail.com) are the co-corresponding authors and the guarantors. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Tables

Table 1. The definition and setting range of parameters in ScEIQRsh model

Parameters	Definition	Method	Setting range
Sc	contactable susceptible under the social NPIs	MCMC	[1, 0.01N]
β'	transmission rate, the number of infected people by one infector	MCMC	[1,19]
σ	transition rate from exposure to being contagious	MCMC	[0.27,0.5]
γ	recovery rate of asymptomatic infector	MCMC	[0.04,0.3]
η	hospitalization rate and pace of symptomatic infectors	MCMC	[0.001,0.999]
κ	extent of epidemiological investigations	MCMC	[0,350]
ρ	positive rate of COVID-19 in quarantined people	MCMC	[0,0.1]
ω	transited rate of quarantined people developing to contagious per day	MCMC	[0.07,0.6]
CR	the proportion of contactable susceptible (Sc) under the interventive social prevention	Sc/N	-
Ipd	the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent	1/σ+1/η	-

utI%	the proportion of untraceable infectors, approximately equates to the asymptomatic	γ/(η+κρη+γ).	-
SurveyQ	the quality of contact tracing	κ•ρ	-
Cpd	the time for untraceable infectors with contagious among susceptible	1/γ	-

Abbreviation: Ipd: Incubation period; Cpd: communicable period; utI%: Proportion of asymptomatic infectors; N: the total population of a province. * Details in the supplementary methods

Table 2. The median value of parameters and indexes across 29 provinces of Mainland China by the fitted ScEIQRsh model.

Variables	**Median**	**IQR 25%, 75%**	**Range**
β'	10.22	8.47, 12.35	3.29-15.06
σ	0.42	0.40, 0.44	0.33-0.48
γ	0.15	0.10, 0.22	0.05-0.26
η	0.69	0.47, 0.87	0.16-0.97
κ	42.0	27.83, 60.78	5.35-147.79
ρ (%)	0.9%	0.4%-1.6%	0.03%-5.10%
ω	0.12	0.10, 0.15	0.07-0.21
Sc	26.98	13.97, 54.57	5.91-25525.54
CR	6.84E-07	3.77E-07, 1.44E-06	1.64E-07-4.33E-04
Ipd	4.17	3.60, 4.71	3.27-9.62
utI%	14.88%	8.17%, 25.37%	3.92%-34.36%
SurveyQ	0.39	0.22, 0.55	0.04-2.61
Cpd	6.77	4.53, 10.36	3.91-19.90
1/σ	2.39	2.26, 2.56	2.07-3.01

Abbreviation: Ipd: Incubation period; utI%: Proportion of asymptomatic infectors; Cpd: communicable period

Figure legend

Figure 1. The flow diagram of ScEIQRsh epidemiological model

Six compartments: contactable susceptible (Sc), exposed individuals (E), infected individuals who were outsides of the public health measures (I), close contacts being in quarantine (Q), self-recovery individuals (Rs) and the cumulative hospitalized individuals (Rh). The flow velocities between the compartments are indicated.

Figure 2. The fitting curves of confirmed cases and close contacts predicted by ScEIQRsh model from Day 0-the 23rd, Jan, 2020

A: The fitting curves of confirmed cases and close contacts in Beijing, the representing of North China.

B: The fitting curves of confirmed cases and close contacts in Liaoning, the representing of Northeast China.

C: The fitting curves of confirmed cases and close contacts in Jiangxi, the representing of East China.

D: The fitting curves of confirmed cases and close contacts in Guangdong, the representing of South China.

E: The fitting curves of confirmed cases and close contacts in Gansu, the representing of Northwest China.

F: The fitting curves of confirmed cases and close contacts in Sichuan, the representing of Southwest China.

G: The fitting curves of confirmed cases and close contacts in Hubei, the representing of Central China.

Figure 3. The association between air temperature and transmission rates (β') of COVID-19

A, B: A, the transmission rates of COVID-19 among acquaintances for the 29 provinces grouped by geographical regions. B Mapping the transmission rate of COVID-19 in 29 provinces of Mainland China. In figure A and B, the number represents the provinces of each geographical region. North China: 1-5; Northeast China: 6-8; East China: 9-15; Central China: 16-18; South China: 19-21; Northwest China: 22-25; Southwest: 26-29.

C. Mapping the daily mean temperature from the 15th, Jan, 2020 to the 15th, Feb, 2020 in 29 provinces of Mainland China.

D: The association between daily minimum temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

E: The association between daily mean temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

F: The association between daily maximum temperature and the transmission rate, β' of COVID-19 depicted by LOESS. Different color dot represents the temperature of one province.

Figure 4. Evaluation of three NPI measures' effectiveness and the suppositional simulation for the measures function

A: The CR calculated by the model in 28 provinces. In B, C, E, F, H, I figure, the solid curves are the fitted curves through our modeling analysis. The meaning of the dash line curves is the suppositional simulation curves after mandatory adjusting three NPI measures' value with different extent. The small dash line means the up-regulation of the NPI measures' value, and the big dash line means the down-regulation of the NPI measures' value. The red curves representing the compartment of Rh; the purple one representing the Q compartment; the orange one representing the I compartment.

B: When we adjusted the CR with 30%-up or down, the change of Rh, Q and I compartments.

C: When adjusted the CR with 50%-up/down, the change of Rh, Q and I compartments.

D: The hospitalization rate and pace, η, of the 29 provinces.

E: The change of Rh, Q and I compartments after adjustment of η with 30% -up/down.

F: The change of Rh, Q and I compartments after adjustment of η with 50% -up/down.

G: The quality of contact tracing, surveyQ was depicted among 29 provinces.

H: The simulation of Rh, Q and I compartments after adjustment of κ for 1/3 down or 3 times up.

I: The simulation of Rh, Q and I compartments after adjustment of ρ- 1/3 down or 3 times up.

Figure 5. The transmission patterns of COVID-19 under social NPIs and the association of untraceable infectors with surveyQ, η and air temperature.

A: A representative example of intra-family and intra-acquaintance transmission pattern of COVID-19 in Beijing.

B: A representative example of COVID-19 transmission pattern among strangers in a large mall.

C: Stranger-stranger transmission is the blind zone of contact tracing.

D: The median proportion of asymptomatic infectors among 29 provinces.

E: The nonlinear association between the ration of untraceable infectors and surveyQ. Higher surveyQ could reduce the ration of untraceable infectors. But as the surveyQ increasing, the proportion of untraceable infectors would be constant.

F: The nonlinear association between the ration of untraceable infectors and η. Higher η could reduce the ration of untraceable infectors either.

G: The relationship between the ration of untraceable infectors and the daily mean temperature.

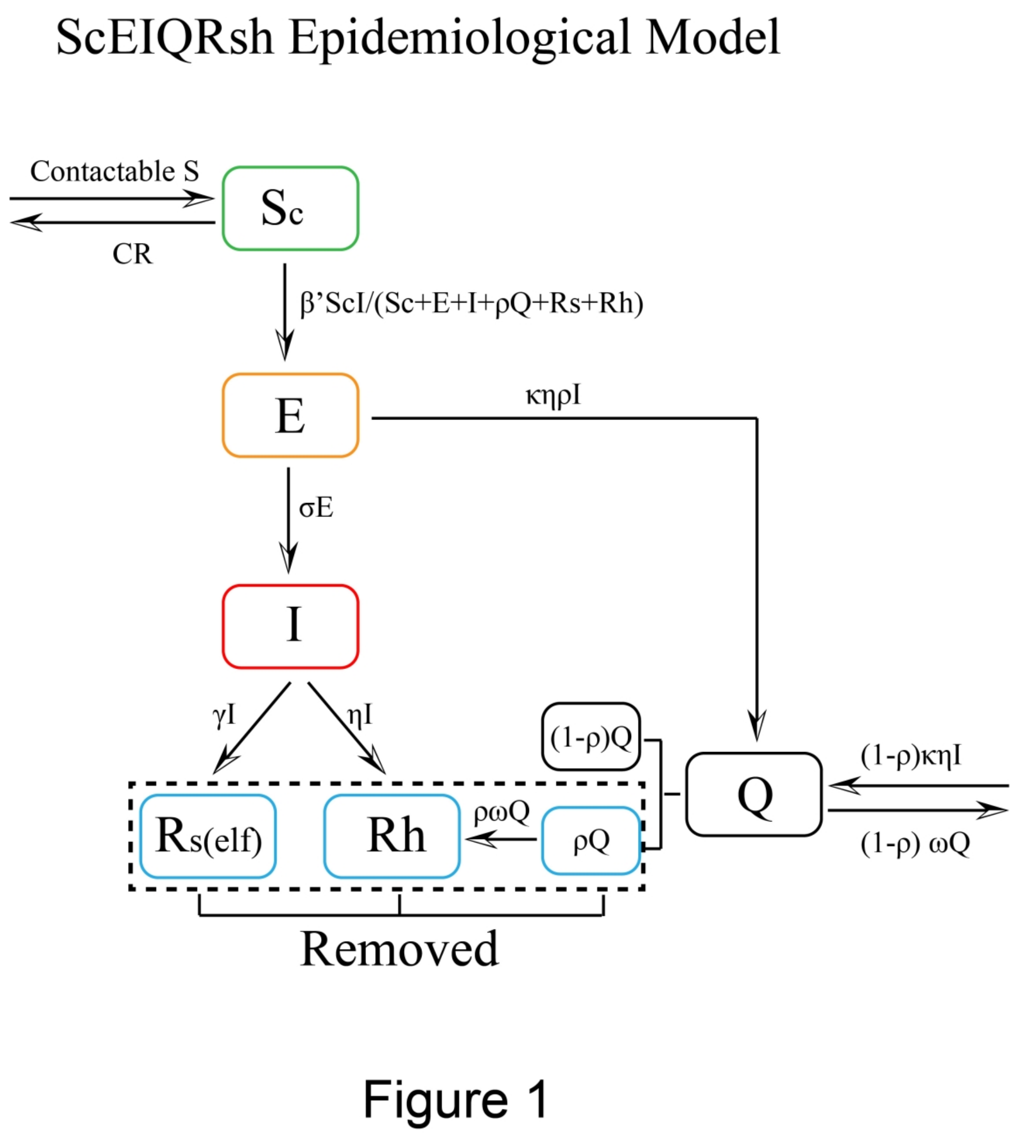

Figure 1

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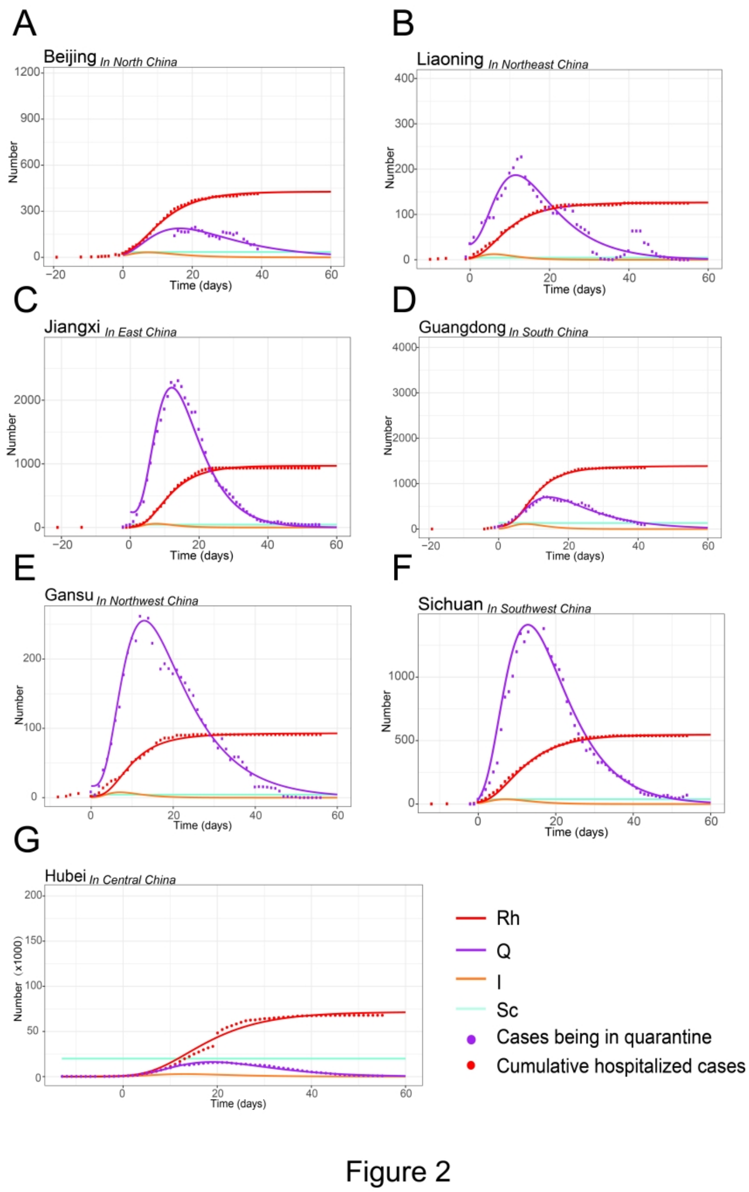

Figure 2

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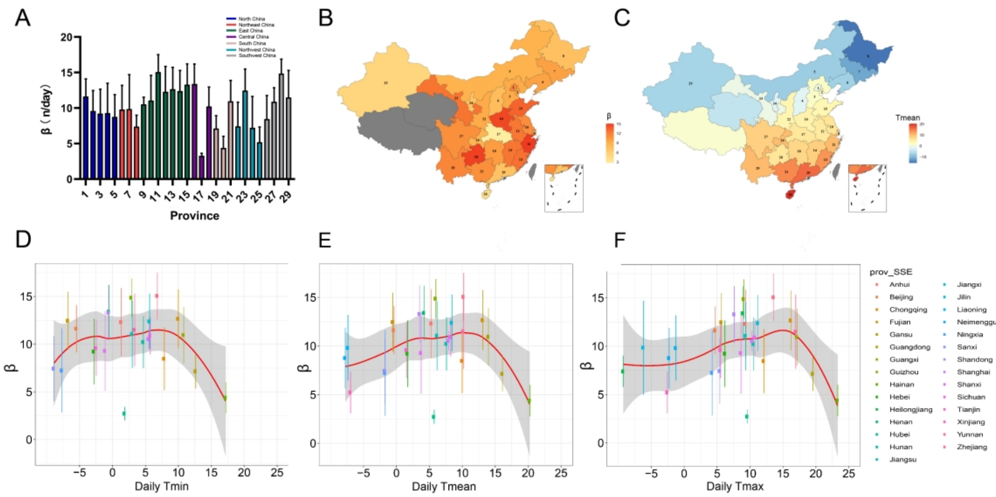

Figure 3

Figure 3

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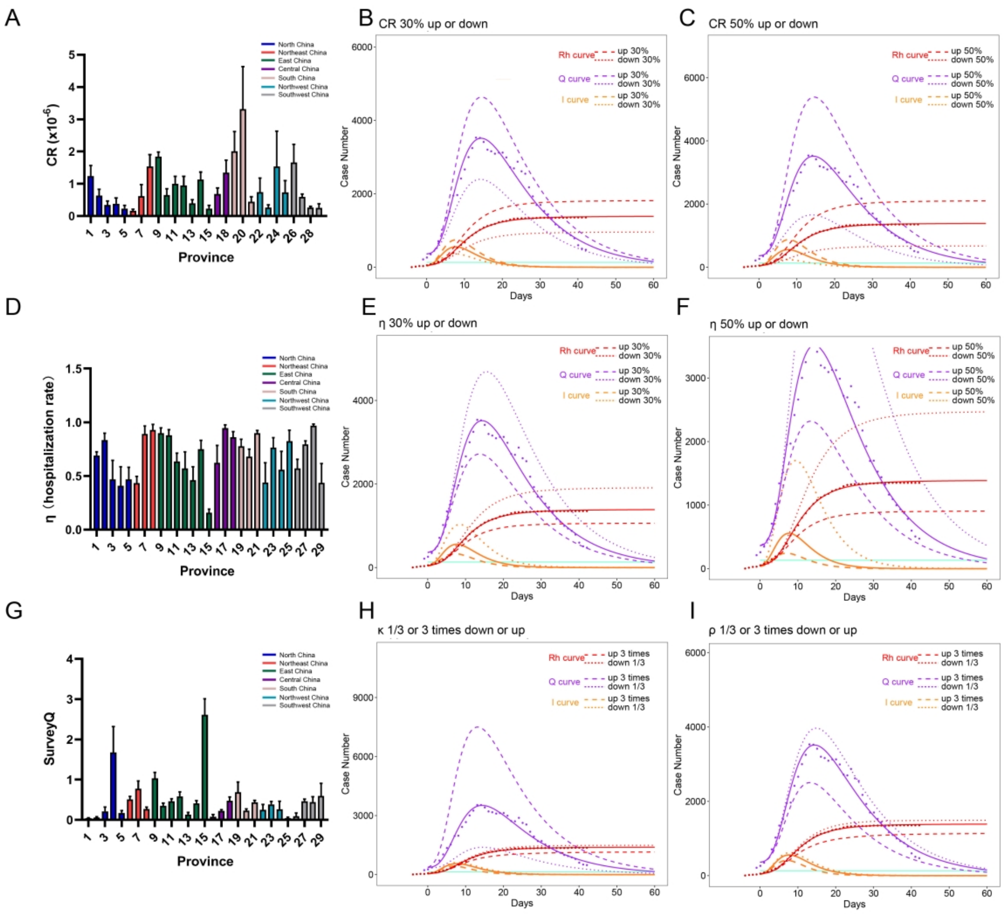

Figure 4

Figure 4

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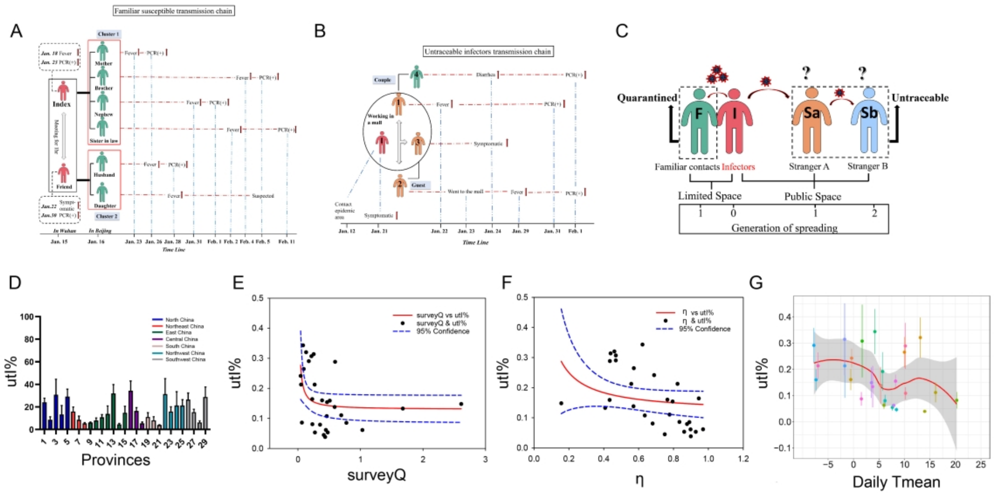


Figure 5

Figure 5

401x218mm (300 x 300 DPI)

The impact of air temperature and containment measures on mitigating the intra-household transmission of COVID-19: a novel data-based comprehensive modeling analysis

Di Liu [*,1], Qidong Tai [*,2], Yaping Wang [3], Miao Pu [3], Lei Zhang [†,2], Bo Su [†,1]

Supplementary methods

The stochastic ScEIQRsh epidemiological model

To simulate the epidemiological data of COVID-19 intra-household transmission under NPIs implementation, we developed an early spreading, early non-pharmaceutical-intervention stochastic model, denoted as ScEIQRsh model. The flow diagram of ScEIQRsh model was as the following, which demonstrated as following:

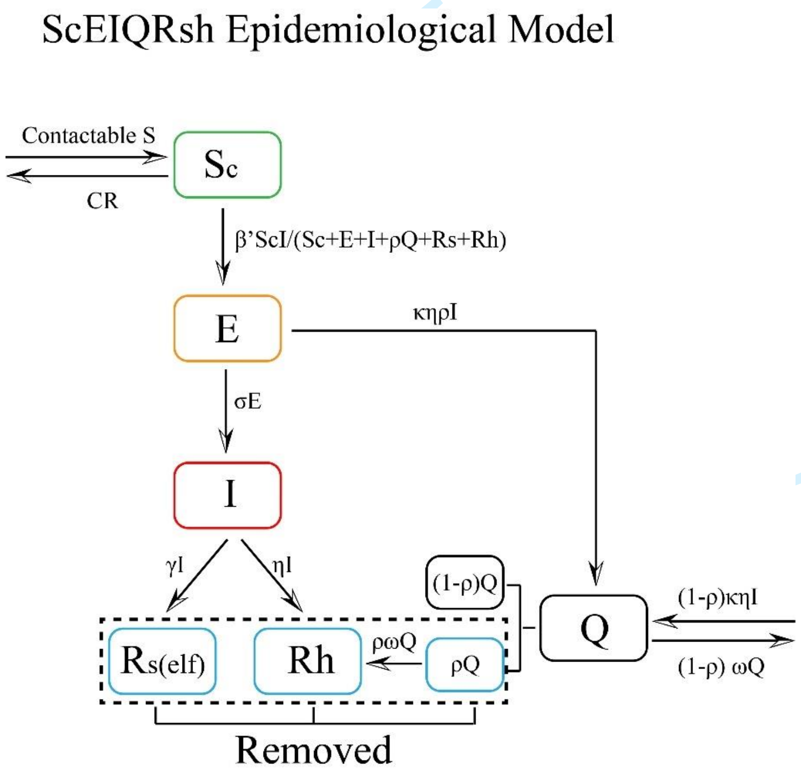


Figure 1

Compartments of the stochastic ScEIQRsh model

Sc: The contactable susceptible subpopulation for the infectors, comprised of their family, relatives, co-workers, friends, and some strangers who could be contacted by the infector under the interventive social prevention. The initial Sc is defined as a continuous random variable with Gaussian distribution in the model. The left arrow of Sc

means the susceptible could be entered into this compartment to become the contactable susceptible (just a part of the susceptible) at the rate of c.

E: The exposed individuals who are in the incubation period after effective contact with the infectors.

I: The infectors, either immigrant or local reproductive infectors who are still outsides of the public health measures.

Q: The close contacts of infectors found out by epidemiological survey, and notified to be in self-quarantine at home, in the hotel or indicated isolating room for 14-day medical observation. The Q value in this model is the daily reported cumulative close contacts or entry of medical observation minus the daily cumulative dismission of medical observation for each province. The right arrow of Q means the quarantined individuals who are not be diagnosed as infectious leave the compartment Q to be the susceptible again at the rate of $(1\text{-}\rho)\ \omega Q$, the opposite arrow means the susceptible in close contacts (in fact, only a small part of close contacts in contact tracing were infected, and the other were still the susceptible) enter the compartment Q at the rate of $(1\text{-}\rho)\kappa\eta I$.

Rs(elf): No all the infectious may see a doctor, especially the non-symptoms infectors. Some of the COVID-19 cases can be self-healing. Thus, the self-recovery individuals who have never be diagnosed and hospitalized because of mild symptoms, or asymptomatic infection, and thus were not be recorded in the daily official epidemic reports is designated as Rs.

Rh: The cumulative individuals who were etiologically diagnosed (mostly SARS-CoV-2 RNA rtPCR positive in oropharyngeal swabs, and inconsistent with other clinical symptoms) and hospitalized in isolate wards. The cumulative number includes any hospitalizing, or dead, or cured COVID-19 patients. In China, every confirmed case had been hospitalized in isolation wards, he/she cannot infect others, so can be regarded as removed.

Removed: The removed means any infectors who have been deprived of the ability to propagate, either by the gain of immunity (Rs, cured in Rh) or by public health measures (infectors in Q, the hospitalizing in Rh), or death (the dead in Rh). The removed in this model is the sum of cumulative Rs, Rh, and the positive cases in Q. So, the flow velocity to Rs and Rh was different.

Model validation

The value of parameters was randomly sampled with one of MCMC method, Metropolis-Hastings (M-H) algorithm, and documented under an appropriate tolerance of best fitting with at least 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for every province of Mainland China.

Other indexes

CR： restriction factor, the proportion of contactable susceptible (Sc) over the total population of a province under the interventive social prevention, which is simply calculated as Sc/N.

utI%: the proportion of the self-recovery removed, including asymptomatic infections or any infection without hospitalization and report, which were estimated as $\gamma/(\eta+\kappa\rho\eta+\gamma)$.

SurveyQ: an estimation for the quality of the epidemical survey, which is calculated as $\kappa \bullet \rho$.

Incubation period: The incubation period was the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent, calculated with $1/\sigma+1/\eta$.

Communicable period: The time for untraceable infectors with contagious among susceptible, calculating with $1/\gamma$.

The air temperature of every province during the COVID-19 outbreak and spreading

The historical meteorological data were collected from china's meteorological administration. The daily mean air temperature was calculated from Jan 15, 2020 to Feb 15, 2020, i.e., from a week before Jan 23, 2020, to 3 weeks after that. In this period, COVID-19 began spreading and controlled by NPI in most of the provinces of China, except Hubei.

The epidemical data and epidemical survey of 31 provinces

The daily confirmed and quarantined cases were used for fitting the model. Almost all the diagnosed cases were hospitalized in isolation wards simultaneously according to the Guidance, thus the reported confirmed cases were just the hospitalized infectors in China. Cases confirmed with a laboratory test of the same sample identified two targets positive detection with real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assay or high-throughput sequencing, one is ORF, another one is the N protein of SARS-CoV-2. The quarantined cases were the population close contact the confirmed cases, asymptomatic infections, and suspected cases identified with epidemiological investigation within 24 hours. The close contacts were including:

1) living, studying, working in the same house with the confirmed or suspected cases.

2) medical staff, family members, or other persons who have close contact with cases in the process of diagnosis, treatment, or nursing.

3) take the same transport and have close contact with infectors, including caregivers, peers, or other passengers(*31*).

The quarantined people were isolated in the home or a specific place for observation of their symptoms for 14 days. If the lab testing results of close contacts of confirmed cases and asymptomatic infections are negative during the medical observation period, they still need to continue quarantine until the end of the observation of 14 days. Those who are in close contact with suspected cases can be relieved of medical observation when suspected cases are excluded from infection.

The provinces of China

There are 34 provincial-level administrative divisions of China, including 23 provinces, 4 municipalities (Beijing, Tianjin, Shanghai, Chongqing), 5 autonomous regions (Guangxi, Inner Mongolia, Tibet, Ningxia, Xinjiang) and 2 special administrative regions (Hong Kong, Macau). 23 provinces are including Anhui, Fujian, Gansu, Guangdong, Guizhou, Hainan, Hebei, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Liaoning, Qinghai, Shaanxi, Shandong, Shanxi, Sichuan, Yunnan, Zhejiang, Taiwan. Seven geographical regions were classified as Mainland

China, named as North China, Northeast China, East China, Central China, South China, Northwest China, Southwest China. The 29 provinces were included in our study, and they were separated into each geographical region and represented by numbers as follows:

1) North China: Beijing, Tianjin, Hebei, Shanxi, Inner Mongolia (1-5);

2) Northeast China: Liaoning, Jilin, Heilongjiang (6-8);

3) East China: Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong (9-15) and Taiwan;

4) Central China: Henan, Hubei, and Hunan (16-18);

5) South China: Guangdong, Hainan, Guangxi (19-21), Hongkong, and Macau;

6) Northwest China: Shaanxi, Gansu, Ningxia, Xinjiang (22-25) and Qinghai;

7) Southwest China: Chongqing, Sichuan, Guizhou, Yunnan (26-29), and Tibet.

Supplementary tables

Table S1. The mean value of parameters and indexes in each province of Mainland China

	Parameters and indexes (Mean±SD)									
Province	**β'**	**σ**	**γ**	**η**	**κ**	**ρ(%)**	**ω**	**CR**	**Ipd (day)**	**utI%**	**Survey Q**
All provinces	10.01±2.86	0.42±0.04	0.16±0.07	0.68±0.20	45.55±28.66	1.32±1.30	0.12±0.03	1.58E-05±7.88E-05	4.31±1.18	15.63±9.27	0.46±0.53
Beijing	11.63±2.48	0.35±0.02	0.23±0.05	0.69±0.04	5.59±0.17	0.78±0.12	0.07±0	1.24E-06±3.24E-07	4.34±0.19	24.22±3.57	0.04±0.01
Tianjin	9.58±2.89	0.33±0.03	0.08±0.03	0.83±0.06	12.79±0.72	0.49±0.12	0.07±0	6.35E-07±1.95E-07	3.71±0.3	8.7±2.58	0.06±0.02
Hebei	9.22±3.44	0.41±0.06	0.22±0.06	0.47±0.18	46.56±6.34	0.47±0.24	0.16±0.02	3.38E-07±1.27E-07	5.05±1.07	30.75±13.89	0.22±0.11
Shanxi	9.29±4.2	0.41±0.05	0.14±0.07	0.41±0.18	65.78±15.26	2.49±0.57	0.14±0.02	3.77E-07±1.82E-07	3.89±1.29	13.35±7.9	1.68±0.64
Neimenggu	8.77±3.12	0.44±0.03	0.22±0.04	0.47±0.11	62.99±5.38	0.27±0.08	0.15±0.01	2.34E-07±9.11E-08	4.55±0.59	29.11±6.61	0.17±0.06
Liaoning	9.81±3.38	0.48±0.02	0.13±0.04	0.43±0.06	27.96±1.68	1.82±0.27	0.12±0.01	1.64E-07±5.09E-08	4.46±0.35	15.98±4.01	0.51±0.08
Jilin	9.85±4.85	0.41±0.06	0.15±0.06	0.89±0.07	58.58±14.51	1.35±0.28	0.13±0.03	6.15E-07±3.60E-07	3.6±0.38	8.62±3.27	0.77±0.2
Heilongjiang	7.39±1.62	0.44±0.03	0.07±0.01	0.93±0.05	27.83±1.98	0.98±0.16	0.11±0.01	1.53E-06±3.76E-07	3.35±0.19	5.43±0.73	0.27±0.05
Shanghai	10.53±1.01	0.41±0.07	0.12±0.01	0.9±0.05	64.41±2.25	1.6±0.19	0.21±0.02	1.84E-06±1.44E-07	5.44±0.54	6.22±0.42	1.03±0.15
Jiangsu	11.06±3.55	0.44±0.04	0.1±0.03	0.88±0.05	32.43±3.1	1.08±0.12	0.15±0.01	6.53E-07±1.96E-07	3.45±0.24	8.01±2.27	0.35±0.06
Zhejiang	15.06±2.46	0.48±0.02	0.11±0.03	0.64±0.08	34.64±2.55	1.33±0.16	0.1±0.01	1.00E-06±2.37E-07	3.67±0.24	10.83±2.35	0.46±0.06
Anhui	12.31±3.55	0.38±0.03	0.14±0.07	0.57±0.15	36.65±4.4	1.61±0.29	0.13±0.01	9.51E-07±2.86E-07	4.55±0.55	13.88±7.03	0.59±0.11

Fujian	12.66±3.09	0.45±0.03	0.23±0.04	0.46±0.12	42.01±2.93	0.31±0.14	0.13±0.01	3.89E-07±1.17E-07	4.55±0.61	32.08±7.71	0.13±0.06
Jiangxi	12.38±2.91	0.41±0.03	0.05±0.01	0.75±0.08	48.15±2.52	0.86±0.11	0.16±0.01	1.13E-06±2.36E-07	3.81±0.18	4.59±0.8	0.41±0.07
Shandong	13.3±2.94	0.35±0.06	0.1±0.06	0.16±0.03	51.26±3.2	5.09±0.69	0.08±0.01	2.36E-07±9.04E-08	9.62±1.3	14.88±5.82	2.61±0.4
Henan	13.4±2.8	0.45±0.03	0.26±0.03	0.62±0.16	24.87±2.71	0.31±0.18	0.12±0.01	6.84E-07±1.90E-07	4.56±0.95	34.36±8.6	0.08±0.05
Hubei	3.29±0.34	0.42±0.05	0.23±0.04	0.95±0.03	5.35±0.62	4.28±0.48	0.11±0.01	4.33E-04±8.35E-05	3.48±0.29	16.49±2.9	0.23±0.03
Hunan	10.22±2.73	0.45±0.03	0.07±0.01	0.86±0.05	38.98±2.47	1.22±0.2	0.16±0.01	1.35E-06±3.82E-07	3.42±0.19	5.44±1.2	0.48±0.09
Guangdong	7.14±1.79	0.44±0.04	0.16±0.06	0.78±0.06	14.33±1.33	4.87±1.82	0.17±0.02	2.01E-06±6.07E-07	3.58±0.26	11.14±3.78	0.69±0.25
Hainan	4.39±1.63	0.44±0.04	0.07±0.03	0.68±0.07	23.03±1.83	1±0.18	0.08±0.01	3.32E-06±1.31E-06	3.78±0.25	8.17±3.17	0.23±0.05
Guangxi	10.95±2.94	0.46±0.02	0.05±0	0.9±0.03	52.88±2.53	0.82±0.08	0.11±0	4.45E-07±1.51E-07	3.27±0.13	3.92±0.3	0.43±0.05
Shaanxi	7.44±3.41	0.4±0.05	0.22±0.05	0.44±0.18	76.13±8.4	0.33±0.17	0.1±0.01	7.43E-07±4.38E-07	5.52±1.91	31.44±13.72	0.25±0.13
Gansu	12.46±3.04	0.45±0.03	0.2±0.05	0.76±0.09	41.99±3.6	0.92±0.14	0.1±0.01	2.66E-07±7.72E-08	3.56±0.27	16.08±4.02	0.39±0.07
Ningxia	7.24±4.41	0.36±0.06	0.17±0.07	0.56±0.17	70.9±11.44	0.37±0.26	0.11±0.02	1.53E-06±1.10E-06	4.91±1.29	21.31±12.15	0.27±0.19
Xinjiang	5.21±2.13	0.41±0.05	0.23±0.05	0.82±0.1	147.79±11.06	0.03±0.01	0.08±0	7.34E-07±3.67E-07	3.71±0.32	21.32±5.08	0.05±0.02
Chongqing	8.47±3.31	0.42±0.03	0.22±0.04	0.57±0.08	39.36±6.01	0.22±0.16	0.13±0.01	1.66E-06±5.67E-07	4.17±0.34	26.52±5.82	0.09±0.08
Sichuan	10.9±1.96	0.38±0.03	0.21±0.04	0.79±0.03	46.84±3.25	0.99±0.07	0.12±0.01	5.92E-07±9.07E-08	3.89±0.22	15.47±2.48	0.47±0.05
Guizhou	14.87±2.03	0.35±0.03	0.09±0.02	0.97±0.02	23.7±3.5	1.86±0.37	0.17±0.02	2.63E-07±3.44E-08	3.92±0.25	6.25±1.45	0.45±0.13
Yunnan	11.49±3.82	0.44±0.04	0.25±0.04	0.44±0.18	97.33±33.65	0.59±0.19	0.15±0.04	2.60E-07±1.18E-07	5.14±1.62	28.89±8.82	0.59±0.31

Abbreviation: Ipd: Incubation period; utI%: Proportion of Untraceable infectors;

Supplementary figure legend

Figure S1. The fitting curves of both the number of daily cumulative confirmed cases and close contacts being in quarantine in 22 provinces of Mainland China (Day 0, the 23rd, Jan, 2020).

A: The fitting curve of provinces in Northwest China- Xinjiang/ Shaanxi/ Ningxia and Central China-Hunan/ Henan.

B: The fitting curve of provinces in South China- Hainan/ Guangxi, and Southwest China-Yunnan/ Guizhou/ Chongqing.

C: The fitting curve of provinces in East China- Shanghai/ Zhejiang/ Anhui/ Fujian/ Shandong/ Jiangsu.

D: The fitting curve of provinces in North China- Neimenggu/ Tianjin/ Hebei/ Shanxi and Northeast China-Heilongjiang/ Jilin.

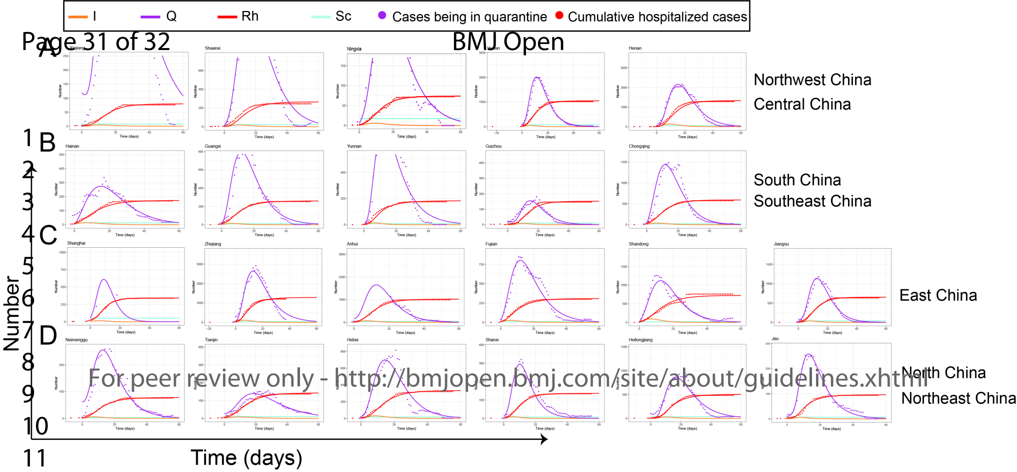
Figure S2. Suppositional simulation of contact tracing parameters, κ and ρ.

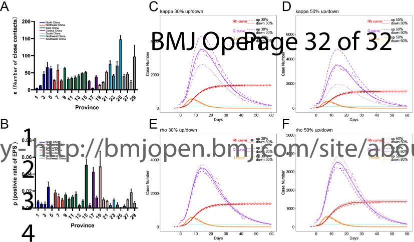
A-B: The median κ and ρ was observed as different among 29 provinces.

C-D: The influence on Rh, Q and I compartment after adjustment of κ by 30% or 50%.

E-F: The simulated Rh, Q and I compartment after adjustment of ρ by 30% or 50%.

Figure S3. The median incubation period of COVID-19 among 29 provinces.


I
Q
Rh
Sc
Cases being in quarantine
Cumulative hospitalized cases
A
Xinjiang
Shaanxi
Ningxia
Hunan
Henan
Northwest China
Central China
B
Hainan
Guangxi
Yunnan
Guizhou
Chongqing
South China
Southeast China
C
Shanghai
Zhejiang
Anhui
Fujian
Shandong
Jiangsu
East China
D
Neimenggu
Tianjin
Hebei
Shanxi
Heilongjiang
Jilin
North China
Northeast China
Number
Time (days)


A
κ (Number of close contacts)
North China
Northeast China
East China
Central China
South China
Northwest China
Southwest China
Province
B
ρ (postive rate of EPS)
Province
C
kappa 30% up/down
Rh curve
Q curve
up 30%
down 30%
Case Number
Days
D
kappa 50% up/down
up 50%
down 50%
E
rho 30% up/down
I curve
F
rho 50% up/down

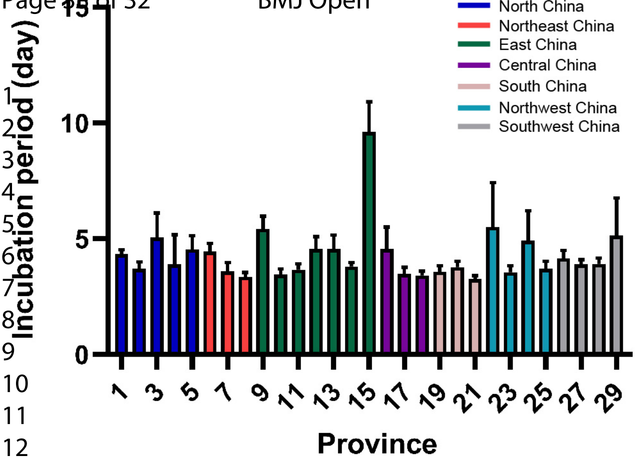

Incubation period (day)
15
10
5
0
North China
Northeast China
East China
Central China
South China
Northwest China
Southwest China
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
Province

Figure S3

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The impact of air temperature and containment measures on mitigating the intra-household transmission of COVID-19: a novel data-based comprehensive modeling analysis

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The impact of air temperature and containment measures on mitigating the intra-household transmission of COVID-19: a novel data-based comprehensive modeling analysis

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Abstract

Objectives

Because of the implementation of non-pharmaceutical interventions (NPIs), the transmission pattern of COVID-19 was changed to intra-household spreading. As the second wave of COVID-19 pandemic worldwide, it was necessarily to re-estimate the influence of temperature on COVID-19 transmission, especially on intra-household transmission.

Design, setting and participates

This is a data-based comprehensive modeling analysis. We established a stochastic epidemiological model (susceptible-Exposed-Infected-Quarantined-Removed model (ScEIQRsh)) to evaluate the influence of air temperature and containment measures on intra-household spreading of COVID-19. The epidemical data of COVID-19 were collected from health commission of Mainland China.

Outcome measures

The model was fitted by Metropolis-Hastings (M-H) algorithm, one Markov Chain Monte Carlo (MCMC) method with a cost function based on least squares method. The LOESS regression was used to depict the relationship between the air temperature and COVID-19 transmission rate in ScEIQRsh model.

Results

We found that the COVID-19 transmission was influenced by air temperature through this ScEIQRsh model, which showed the optimal temperature range of 5℃-14℃ (41°F-57.2°F) and peak of 10℃ (50°F) for COVID-19 spreading. From fitted model, the fitted intra-household transmission rate (β') of COVID-19 was 10.22 (IQR 8.47, 12.35) across Mainland China. The association between air temperature and the β' of COVID-19 suggests that COVID-19 pandemic might be seasonal. The effectiveness of NPIs was also validated by our model, which demonstrated that the measures to diminish contactable susceptible (Sc), and to avoid delay of diagnosis and hospitalized isolation (η) were more effective than contact tracing (κ, ρ). But the most effectual way for ultimate COVID-19 control is vaccination.

Conclusions

We constructed a novel epidemic model to estimate the impact of air temperature on COVDI-19 transmission beside the NPIs' implementation, which can be helpful for decision making of public health strategy, and prediction of the COVID-19 transmission or other infectious disease in the future.

Strengths and limitations of this study

A novel epidemiological susceptible-Exposed-Infected-Quarantined-Removed model (ScEIQRsh) established.

The Metropolis-Hastings (M-H) algorithm, one Markov Chain Monte Carlo (MCMC) method utilized.

Exploring the influence of air temperature on COVID-19's intra-household transmission.

Using the epidemical date of Mainland China for model validation.

Introduction

The COVID-19 has been spread for more than one year in many countries. There are many factors, such as the virus virulence, the host defense potential, the number of contacts *et al* that could impact the transmission[1]. Among them, the air temperature might be one important factor for impacting the transmission of SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2), which cause the COVID-19 epidemic, since the influenza virus was affected by the changes of temperature and relative humidity[2]. However, the meteorological indicators impact on COVID-19 transmission is unclear. A few studies reported the air temperature influence COVID-19 pandemic. Bilal and the colleagues found the temperature was significant associated with the COVID-19 pandemic in USA[3 4] and Germany[5] as well. But some researchers published the adverse conclusion[6 7]. It is controversial for the impact of air temperature on COVID-19 transmission.

In the past year, many countries' government implemented non-pharmaceutical interventions (NPIs), including physical and social distancing, quarantine, and isolation to impede the COVID-19 outbreak in the early stage[8]. In China, the pandemic of COVID-19 was prevented within two months under those NPIs executed since Jan 23, 2020. Besides the announcement of keeping physical and social distance to the public, epidemiological survey (EPS) -based quarantine and hospitalized isolation were applied [9]. These containment measures were effective for controlling the spreading of COVID-19. But, what's the influence of temperature on the COVID-19 incidence and transmission besides the NPIs' effect?

We then used the data from China as an appropriate example to evaluate the relationship between the air temperature and COVID-19 spreading. Firstly, the social intervention in China is almost taken at the same time and is almost uniform with different intensity between provinces. Secondary, the latitude span of mainland China is large enough to reflect the zones with daily mean air temperature of -7℃ to 20℃ in winter. At last, we could get the completely data of the daily numbers of cases in quarantine by contact tracing for each province. Thus, we constructed a new kind of SEIR (Susceptible-Exposed-Infected-Removed)-based model, named ScEIQRsh (Contactable Susceptible-Exposed-Infected-Quarantined-Removed) to depict a new spreading pattern of COVID-19, the intra-household transmission. Which can separate the influence of social intervention measures from confounding factors, and with machine learning methods we achieved the precise influence of air temperature on COVID-19 spreading. Also, the effectiveness of the NPIs on control the COVID-19 transmission was validated by this model as well.

Materials and Methods

Development of the dynamical non-classical SEIR model for COVID-19

The developed ScEIQRsh model is an expanded model from classic SEIR epidemic model, which contains six compartments named as Sc (contactable susceptible), E (the exposed to SARS-COV-2), Q (daily close contacts being in quarantine), I (infectors outside of the healthcare system), Rh (accumulative hospitalized infectors), and Rs (self-recovery individuals with asymptomatic infection or mild symptoms who have never be hospitalized and registered in healthcare system) (Figure 1). Sc represents the contactable susceptible under the social NPIs, such as lockdown, social distancing, cancelling gatherings, closing public places, which is set as a random variable in the model. Q reflects the contact tracing (CCT) for quarantine, and Rh reflects the confirmed and hospitalized infectors in isolation wards, and this kind of population was daily reported by public health agency. E, I, and Rs compartments were outside of the healthcare system. Rh is really the reported cumulative confirmed cases in the model. Every compartment has been linked by a few parameters, and the flow velocity of each compartment is illustrated in figure 1 (details in the supplementary methods).

Parameters of the stochastic ScEIQRsh model

The definition and initial range of model parameters of β', σ, γ, κ, ρ, ω, η and Sc in the model were listed in Table 1. β' was the intra-household transmission rate dependent of the property of SARS-COV-2. σ and γ were associated with the intrinsic incubation period and communicable period of COVID-19. κ, ρ and ω were associated with contact tracing and quarantine. η reflected the pace of confirmed diagnosis and hospitalized isolation for infectors. Other indexes could be calculated from the solved model, such as the contact rate (CR), the quality of CCT (surveyQ), the proportion of untraceable infectors (approximately equate to the asymptomatic) (utI%), the incubation period and communicable period of SARS-COV-2, and among them, CR reflects the proportion of Sc in population under the integrated NPIs, surveyQ represents the quality of contact tracing.

β': the effective intra-household transmission rate for the contactable susceptible (Sc).

σ: the progression rate from exposed to being infectious, which is the reciprocal of the incubation period (days) in the propagate chain.

γ: the removal rate for Rself, which is the reciprocal of the apparent period of being propagating for a self-recovery infector in the propagate chain.

η: the removal rate for Rh, which is the reciprocal of the apparent period of being propagating for a hospitalized infector in the propagate chain.

κ: the average number of traceable close contacts for each confirmed case, which was investigated and notified to be in quarantine by the epidemiological survey group of each province. All the found close contacts were assumed to be in a 14-day quarantine.

ρ: the virus-positive rate of the individuals in quarantine for each province.

ω: the dismiss rate of virus-negative individuals in quarantine

Formulation and Parameters setting of ScEIQRsh model

The simultaneous differential equations system for the stochastic ScEIQRsh model is as follows:

(1) $dE/dt = \beta' Sc I/(Sc+E+I+Rs+Rh+\rho Q) - \kappa\eta\rho I - \sigma E$;

(2) $dI/dt = \sigma E - \eta I - \gamma I$;

(3) $dQ/dt = \kappa\eta I - \omega Q$;

(4) $dRh/dt = \eta I + \rho\omega Q$;

(5) $dRs/dt = \gamma I$;

* In equation (1), unlike the classical SIR or SEIR model, the denominator of flow-in velocity is ($Sc+E+I+Rs+Rh+\rho Q$) instead of N or any other constants. The denominator means all the transmitted individuals in the system. The classical SIR or SEIR model assumes that the infectors mix up with different susceptible every day, and ScEIQR model assumes that the infectors mix up with the fixed contactable susceptible every day.

The parameters setting: β', σ, γ and η were set as random variables with Gaussian distribution; κ, ω, ρ was set as random variables with uniform distribution. Parameters range setting: β' [1,19], σ [0.27,0.5], γ [0.04,0.3], η [0.001,0.999], κ [0,350], ω [0.07,0.6], ρ [0,0.1].

Sc was set as a random variable with Gaussian distribution and the range setting was Sc(0,0.002N]. N denotes the total population of the province. The other initial compartment values were estimated as the following: initial Rh=H0, initial Rs=0, initial Q=Q0, initial $I=H0*(1-\eta)/\eta$, initial E= initial I/σ. H0, Q0 denotes the cumulative hospitalized cases, close contacts in quarantine at Day 0 (23rd, Feb 2020) reported by the public health administration of the province. If H0 or Q0 is missing for some province, H0 or Q0 will be given an assumed number.

Acquisition the epidemic data

The intra-household and intra-household transmission of COVID-19 [10] could be observed at the beginning of COVID-19 spreading in Mainland China [11]. And each Provincial Health Commission would report the daily number of close contacts being in quarantine besides reporting the number of daily confirmed cases of COVID-19. This completed data of Mainland China was good for fitting the ScEIQRsh model and investigating the intra-household or intra-acquaintances transmission of COVID-19. We collected the data of daily accumulative confirmed cases of COVID-19 from January to March, 2020 through the 31 Provincial Health Commission of Mainland China. The daily number of close contacts in quarantine and the daily number of whom were relieved of quarantine were also collected from the provincial government website in China. Xizang and Qinghai province were excluded because of few cases, with only one and 18 confirmed cases, respectively. Almost all the diagnosed cases were hospitalized in isolation wards simultaneously according the Guidance, thus the reported confirmed cases were just the hospitalized infectors in China. Details of the criteria of confirmed cases and close contacts in quarantine were clarified in the supplementary methods.

Simulation and model fitting

We fitted both the reported accumulative confirmed cases and daily close contacts in quarantine with Rh and Q compartments by ScEIQRsh model for each province by Markov Chain Monte Carlo (MCMC) method with a cost function based on least squares method. Briefly, model parameters and Sc were random samplings with Metropolis-Hastings (M-H) algorithm, one of Markov Chain Monte Carlo (MCMC) method. The proposal distribution for accept-reject is a Bernoulli distribution from the comparison of the cost function of curve fitting in iteration (better or not). Both simulated curves of Rh and Q were simultaneously fitted with the raw data (the real word data) by the least-squares method. And the cost function was SSE/SST (Sum of Squares for Error/Sum of Squares for Total). The optimized parameters were documented with 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for 29 provinces of Mainland China. The expected value and standard deviation for each parameter were then confirmed.

Air temperature of provinces in China during the COVID-19 spreading

The minimum (Tmin), mean (Tmean), maximum (Tmax) air temperature of each province was collected from the National Meteorological Administration from Jan 15, 2020 to Feb 15, 2020 (one week before and three weeks later of Jan 23, 2020 (Day 0)). The LOESS regression was used to depict the relationship between the air temperature of 29 provinces and COVID-19 transmission rate in ScEIQRsh model.

Patient and Public Involvement

No patient involved.

Statistical analysis

The enrolled 29 provinces for model validation were separated into seven geographical regions, named as North, Northeast, East, Central, Northwest, South and Southwest China. The curves of Rh and Q were simultaneously fitted with the raw data by least squares method with tolerance of 1.05. SSE/SST (Sum of Squares for Error/Sum of Squares for Total) as the cost function. The data process was performed on R (version 3.6.1), and the "deSolve" R package was used as the solver of differential equations. The R source code can be found in *GitHub*. The parameters were denoted as mean±SD for each province, and the median (interquartile range, IQR: 25%, 75%) was used for describing across provinces.

Results

The influence of air temperature on the transmissibility of COVID-19

The intra-household transmission rate (β') was calculated first, and then the nonlinear association between β' and air temperature was depicted by LOESS fitting.

The intra-household transmission rate (β') calculated

Firstly, we fit the COVID-19 transmission with integrated social NPIs by the ScEIQRsh model, which can be well fitted with both the reported number of daily accumulative confirmed cases and close contacts being in quarantine in 29 provinces of Mainland China (Figure 2, Figure S1). The predicted daily Rh and Q compartments were coincident with the provincial reported numbers. From the fitting curves, we obtained the median intra-household transmission rate (β') for 29 provinces were 10.22 (IQR 8.47, 12.35), which implied about 10.22 person would be infected by one infector in case that the susceptible are mostly acquaintances and Sc is extrapolated to infinite (Figure 3A-B, Table 2, Table S1).

The rang of air temperature for COVID-19 spreading

The span of mean air temperature for every province in China was from -15 °C (5 °F) to 20.25 °C (68.45 °F) during the COVID-19 spreading period of Jan to Feb 2020 in China (Figure 3C). The relationship between the air temperature and β' was evaluated. As the daily air temperature increased from subzero (0°C, 32°F), the value of β' raised gradually until the air temperature went up to a peak of 7°C (44.6°F) for minimum daily temperature, 10°C (50°F) for mean or 15°C (59°F) for maximum daily temperature, respectively (Figure 3D, E, F), and then declined sharply as the temperature continued to raise. We observed transmission rate (β') was higher than 11 in the range of 5℃-14℃ (41°F-57.2°F) for mean air temperature, which may be most suitable for COVID-19 spreading.

Validation the NPIs on mitigating the COVID-19 spreading

The second wave of COVID-19 pandemic is appearing in many countries currently because of the coronavirus mutation. But the containment measures are still pivotal for controlling COVID-19 spreading.

Assessment of NPI measures by suppositional simulation

We mainly assessed three independent parameters, contact rate (CR), η and surveyQ, which were crucial for stopping the spreading chain. Based on our model, the median Sc was estimated as 26.98 (IQR:13.97, 54.57) with the highest in Hubei and lowest in Neimenggu province (Table S1). The median CR for 29 provinces was accordingly 6.84E-07 (IQR 3.77E-07, 1.44E-06) (Figure 4A). To illustrate the influence of NPI measures on COVID-19 transmission for ScEIQRsh model, we arbitrarily adjusted CR, κ, ρ, and η value with representative 30% or 50% up/down-regulation to simulate the suppositional spreading situation. If CR were 30% or 50% enlarged, the eventual accumulative hospitalized cases (Rh) would strongly increase, the peak of infectors (I) would be brought backward and vice versa (Figure 4B, 4C). The median for velocity of hospitalized isolation for infectors (η) was 0.69 (IQR 0.47, 0.87) among 29 provinces (Figure 4D). The influence of η is the opposite to CR. If the η were increased as 30% or 50%, the eventual Rh would be strongly reduced and vice versa (Figure 4E, 4F).

SurveyQ, the product of κ times ρ, was 0.39 (IQR 0.22, 0.55), which indicated that 0.39 positive cases were found in close contacts of CCT averagely for each confirmed infector (Figure 4G). The κ and ρ can be used to assess the effectiveness of CCT, and the median κ of 29 provinces was 42.0 (IQR 27.83, 60.78), suggesting that 42 close contacts of one infector had been excavated averagely by CCT groups (Figure S2A). The COVID-19 positive rate (ρ) in close contacts was speculated as 0.98% (IQR 0.47%-1.60%), ranged from 0.03%-5.10% (Figure S2B), which was quite close to the WHO-China joint report of 0.9%-5% in China [11]. In case of enlarged κ or ρ, the eventual accumulative number of confirmed COVID-19 would diminish and the plateau of Rh would be brought forward (Figure 4H, 4I, Figure S2C, D, E, F). On the same adjusted amount, the effectiveness of CR and η on spreading prevention were stronger than that of CCT parameters, κ and ρ. The incubation period and communicable period of COVID-19 was calculated by ScEIQRsh model, and the results were consistency with other studies (Table 2, Figure S3), which reflected the reasonable of this novel model.

Blind zone of contact tracing and asymptomatic infectors in NPIs strategy

With the integrated social NPIs, COVID-19 transmission mostly occurred between free infectors and acquaintances, as well as a few strangers whom the infectors have to contact for daily necessities. In a typical intra-householdintra-acquaintance transmission, the index case transmitted to four of his family members and one friend directly, and the friend's family indirectly infected within half a month[12] (Figure 5A). CCT can easily find close contacts of acquaintances, but be inefficient in finding transmission among strangers in public space. For example, a salesman index transmitted to two unacquainted salesmen in other sales areas sequentially without gathering in a large mall, and a customer without any inquiry and purchase was infected by one of the transmitted salesmen after 30-minutes lingering (Figure 5B). This transmission chain in strangers could not be easily found by contact tracing, and was only revealed after all the participants appeared symptoms (Figure 5C).

Another blind spot of contact tracing is about asymptomatic infection. The calculated proportion of asymptomatic and mild-symptom infectors without hospitalization (the proportion of untraceable infectors, utI%) by ScEIQRsh model was 14.88% (IQR 8.17%, 25.37%), ranged from 3.92%-34.36% across 29 provinces, which implied that average 14.88% COVID-19 patients couldn't be found out with social NPIs, and the average proportion of asymptomatic in COVID-19 patients should be smaller than 14.88% (IQR 8.17%, 25.37%) (Figure 5D). The higher surveyQ of CCT can only reduce but not eliminate utI% (Figure 5E), but high η could decline the utI% constantly (Figure 5F). Hence, contact tracing is not sufficient to find all the infectors, especially in stranger-stranger transmission and asymptomatic infection. The ratio of asymptomatic infectors also influenced by air temperature. When the mean air temperature is subzero, the utI% is high (Figure 5G).

Discussion

Whether the meteorological conditions affect the spread of COVID-19 is vitally important in prediction of COVID-19 prevalence, especially for intra-household transmission in the future. In our study, we found the transmission rate (β') increased as the minimum, mean, maximum temperature rose from -5°C (23°F) and reach the peak at 7°C (44.6°F), 10°C (50°F), and 15°C (59°F), respectively, and then started to decline at higher temperature across the 29 provinces in China. It is coincident with the curves reported by Wang Mao *et al*[13], who have claimed that the peak of accumulative cases of 492 cities appeared at the minimum, average and maximum temperature of 6.7°C(44.06°F), 8.72°C(47.7°F) and 12.42°C(54.36°F) respectively. Wang Mao *et al* [13] and Sajadi MM *et al* [14] found that regions in 30-50° N' corridor with 5°C-11°C (41°F-51.8°F) average temperature had increased COVID-19 transmission. We also coincidentally discovered the optimal mean temperature ranges for COVID-19 transmission were 5°C-14°C (41°F-57.2°F). Lowen Ac *et.al* proved that influenza virus transmission by droplets was greater and the peak duration of virus shedding lasted longer at 5°C (41°F) than 20°C (68°F)[15]. Indeed, the β' of COVID-19 at 5°C (7.39±1.62) was higher than β' at 20.25°C (4.39±1.63). Another similar infectious disease, SARS was found with higher transmission in temperature<24.6°C than >24.6°C circumstance in Hong Kong [16]. From the curve we illustrated, we could suspect the transmission rate would further reduce at higher temperature over 20.25°C (68.45 °F), but not eliminate. It can be expected that COVID-19 pandemic spreading would mitigate for the northern hemispheres in the summer, and it is likely to become a seasonal infectious disease from the currently situation. The broader range of air temperature for optimal COVID-19 transmission strongly suggests the necessity and urgency of vaccine at present.

Besides the influence of air temperature, the most important measures to contain the COVID-19 epidemic is the vaccine and the NPIs. After first-level public health emergency response on the Jan 23, 2020, integrated NPIs were implemented in Mainland China during the epidemic of COVID-19 [9]. The spreading pattern of COVID-19 was changed into intra-household transmission. A report of the "WHO-China Joint Mission on COVID-19" verified in Guangdong and Sichuan province, about 78%-85% of intra-household infections were within families [11]. And in Beijing, there are 176 intra-household cases among 262 confirmed cases and 133 (50.8%) were intra-household cases [10]. We estimate the effectiveness of integrated NPIs to simulate COVID-19 restricted spreading among acquaintances for the first time by our ScEIQRsh epidemic model. ScEIQRsh model can well fit the realistic provincial epidemic and NPI data of COVID-19 in China entirely without halfway adjustment of the parameters. Because, unlike the classical SEIR (Susceptible-Exposed-Infected-Removed) epidemic model assumes that infectors mix up with all the susceptible per day, the infectors of ScEIQRsh mix up with the contactable susceptible per day, which indicates the family members, relatives, co-workers, friends and some contactable strangers for obtaining daily necessities of the infectors. Because the contact among acquaintances is more frequent than the contact among the whole population, the β' value is usually larger in our model than that of classical SEIR model in other studies [17].

In those NPIs measures, CR and η are more effective to diminish the eventual accumulative number of COVID-19 cases than CCT parameters κ and ρ. In case of insufficiency of medical resources, the better way to improve η could be enlargement of the laboratory capacity for SARS-COV-2 testing or building makeshift hospitals to increase bed capacity [18]. Contact tracing is also helpful for mitigating COVID-19 spreading, which can be regarded as a reminder to be more precautious for close contacts (quarantine for targeted susceptible) than the common susceptible. The surveyQ (κ•ρ) of CCT could be improved with adding more CCT staffs, loosening the criteria of close contacts in CCT, broadening SARS-COV-2 testing to close contacts, or using digital tools. It is undeniable that above methods require more human and financial resources, and may not be suitable for every country in reality. Nevertheless, lockdown and stay-at-home affects the society and economy seriously, contact tracing is an alternative option with less quarantine and consumptions. In brief, keeping the contactable susceptible (Sc or c) in extremely low level and maintaining η in high level are crucial for COVID-19 control.

Additionally, the asymptomatic infectors with contagiousness are source for recurrence of COVID-19 epidemic. We demonstrated that the median and highest proportion of asymptomatic infectors were 14.88% and 34.36% respectively. It was consistent with the reported 18% in 700 infectors never showed symptoms on *Diamond Princess* by Kenji Mizumoto *et al* [19] and claim of 30.8% asymptomatic cases in 565 Japanese citizens evacuated from Wuhan by Hiroshi Nishiura *et al* [20]. The low air temperature could also increase the proportion of asymptomatic infectors. Hence, the implementation of the containment measures is crucial besides the air temperature influence. Clinically significant features of COVID-19 such as incubation period deducted from ScEIQRsh model are accorded with the reported 3 days in a study of including 1,099 laboratory-confirmed cases by Zhong N.S *et al*[21], which indicates that the model simulates the transmission process in real-word situation.

Our study based on a novel ScEIQRsh NPIs model, and only included the epidemic date of Mainland China for model validation because we cannot access the NPIs data, e.g., close contacts of other countries. This model could be fitted even if the NPIs data is sparse, but with less accuracy. The limited latitude spans made the range of air temperature not so broad, especially for higher temperature, though the association of air temperature with COVID-19 transmission rate was informative and suggestive[22].

Conclusions

In conclusion, we provided a new tool for quantitative assessing the influence of air temperature or the effectiveness of NPIs strategy on COVID-19 outbreak. We also speculated the appropriate temperature for SARS-COV-2 transmission might be within 5℃-14℃ (41°F-57.2°F) under the implementation of NPIs. The stochastic ScEIQRsh model which can well fit both the early spreading and early social intervention data of COVID-19 was constructed. The effectiveness of NPIs for mitigating the transmission of COVID-19 were evaluated. Keeping the contactable susceptible in low level and promoting the diagnosis and hospitalized isolation of COVID-19 promptly are crucial for mitigating early intra-household transmission of COVID-19, which provided new evidence to decision making of effective public health intervention strategy for COVID-19 prevention. This model is also applicable for any other regions because the proportion of acquaintances and strangers could auto-adjust by the fitting process, and it is also suitable for other similar infectious disease.

Ethics statement

This study does not involve human participants. This study does not involve animal subjects.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare no competing interests.

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Contributors

DL and QT are joint first authors, contributed equally to this article for drafting the manuscript. BS and LZ conceived and designed the study. QT, MP and YW collected the epidemiological data of each province in Mainland China. BS and DL analyzed the date with the help of YW and MP. DL and QT drafted the manuscript. BS and LZ revised the manuscript critically. All authors reviewed and approved the final manuscript. LZ (ZHANGLEI_FKYY@163.COM) and BS (subo_group@hotmail.com) are the co-corresponding authors and the guarantors. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Tables

Table 1. The definition and setting range of parameters in ScEIQRsh model

Parameters	Definition	Method	Setting range
Sc	contactable susceptible under the social NPIs	MCMC	[1, 0.01N]
β'	transmission rate, the number of infected people by one infector	MCMC	[1,19]
σ	transition rate from exposure to being contagious	MCMC	[0.27,0.5]
γ	recovery rate of asymptomatic infector	MCMC	[0.04,0.3]
η	hospitalization rate and pace of symptomatic infectors	MCMC	[0.001,0.999]
κ	extent of epidemiological investigations	MCMC	[0,350]
ρ	positive rate of COVID-19 in quarantined people	MCMC	[0,0.1]
ω	transited rate of quarantined people developing to contagious per day	MCMC	[0.07,0.6]
CR	the proportion of contactable susceptible (Sc) under the interventive social prevention	Sc/N	-
Ipd	the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent	1/σ+1/η	-

utI%	the proportion of untraceable infectors, approximately equates to the asymptomatic	$\gamma/(\eta+\kappa\rho\eta+\gamma)$.	-
SurveyQ	the quality of contact tracing	$\kappa \cdot \rho$	-
Cpd	the time for untraceable infectors with contagious among susceptible	$1/\gamma$	-

Abbreviation: Ipd: Incubation period; Cpd: communicable period; utI%: Proportion of asymptomatic infectors; N: the total population of a province. * Details in the supplementary methods

Table 2. The median value of parameters and indexes across 29 provinces of Mainland China by the fitted ScEIQRsh model.

Variables	Median	IQR 25%, 75%	Range
β'	10.22	8.47, 12.35	3.29-15.06
σ	0.42	0.40, 0.44	0.33-0.48
γ	0.15	0.10, 0.22	0.05-0.26
η	0.69	0.47, 0.87	0.16-0.97
κ	42.0	27.83, 60.78	5.35-147.79
ρ (%)	0.9%	0.4%-1.6%	0.03%-5.10%
ω	0.12	0.10, 0.15	0.07-0.21
Sc	26.98	13.97, 54.57	5.91-25525.54
CR	6.84E-07	3.77E-07, 1.44E-06	1.64E-07-4.33E-04
Ipd	4.17	3.60, 4.71	3.27-9.62
utI%	14.88%	8.17%, 25.37%	3.92%-34.36%
SurveyQ	0.39	0.22, 0.55	0.04-2.61
Cpd	6.77	4.53, 10.36	3.91-19.90
1/σ	2.39	2.26, 2.56	2.07-3.01

Abbreviation: Ipd: Incubation period; utI%: Proportion of asymptomatic infectors; Cpd: communicable period

Figure legend

Figure 1. The flow diagram of ScEIQRsh epidemiological model

Six compartments: contactable susceptible (Sc), exposed individuals (E), infected individuals who were outsides of the public health measures (I), close contacts being in quarantine (Q), self-recovery individuals (Rs) and the cumulative hospitalized individuals (Rh). The flow velocities between the compartments are indicated.

Figure 2. The fitting curves of confirmed cases and close contacts predicted by ScEIQRsh model from Day 0-the 23rd, Jan, 2020

A: The fitting curves of confirmed cases and close contacts in Beijing, the representing of North China.

B: The fitting curves of confirmed cases and close contacts in Liaoning, the representing of Northeast China.

C: The fitting curves of confirmed cases and close contacts in Jiangxi, the representing of East China.

D: The fitting curves of confirmed cases and close contacts in Guangdong, the representing of South China.

E: The fitting curves of confirmed cases and close contacts in Gansu, the representing of Northwest China.

F: The fitting curves of confirmed cases and close contacts in Sichuan, the representing of Southwest China.

G: The fitting curves of confirmed cases and close contacts in Hubei, the representing of Central China.

Figure 3. The association between air temperature and transmission rates (β') of COVID-19

A, B: A, the transmission rates of COVID-19 among acquaintances for the 29 provinces grouped by geographical regions. B Mapping the transmission rate of COVID-19 in 29 provinces of Mainland China. In figure A and B, the number represents the provinces of each geographical region. North China: 1-5; Northeast China: 6-8; East China: 9-15; Central China: 16-18; South China: 19-21; Northwest China: 22-25; Southwest: 26-29.

C. Mapping the daily mean temperature from the 15th, Jan, 2020 to the 15th, Feb, 2020 in 29 provinces of Mainland China.

D: The association between daily minimum temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

E: The association between daily mean temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

F: The association between daily maximum temperature and the transmission rate, β' of COVID-19 depicted by LOESS. Different color dot represents the temperature of one province.

Figure 4. Evaluation of three NPI measures' effectiveness and the suppositional simulation for the measures function

A: The CR calculated by the model in 28 provinces. In B, C, E, F, H, I figure, the solid curves are the fitted curves through our modeling analysis. The meaning of the dash line curves is the suppositional simulation curves after mandatory adjusting three NPI measures' value with different extent. The small dash line means the up-regulation of the NPI measures' value, and the big dash line means the down-regulation of the NPI measures' value. The red curves representing the compartment of Rh; the purple one representing the Q compartment; the orange one representing the I compartment.

B: When we adjusted the CR with 30%-up or down, the change of Rh, Q and I compartments.

C: When adjusted the CR with 50%-up/down, the change of Rh, Q and I compartments.

D: The hospitalization rate and pace, η, of the 29 provinces.

E: The change of Rh, Q and I compartments after adjustment of η with 30% -up/down.

F: The change of Rh, Q and I compartments after adjustment of η with 50% -up/down.

G: The quality of contact tracing, surveyQ was depicted among 29 provinces.

H: The simulation of Rh, Q and I compartments after adjustment of κ for 1/3 down or 3 times up.

I: The simulation of Rh, Q and I compartments after adjustment of ρ- 1/3 down or 3 times up.

Figure 5. The transmission patterns of COVID-19 under social NPIs and the association of untraceable infectors with surveyQ, η and air temperature.

A: A representative example of intra-family and intra-acquaintance transmission pattern of COVID-19 in Beijing.

B: A representative example of COVID-19 transmission pattern among strangers in a large mall.

C: Stranger-stranger transmission is the blind zone of contact tracing.

D: The median proportion of asymptomatic infectors among 29 provinces.

E: The nonlinear association between the ration of untraceable infectors and surveyQ. Higher surveyQ could reduce the ration of untraceable infectors. But as the surveyQ increasing, the proportion of untraceable infectors would be constant.

F: The nonlinear association between the ration of untraceable infectors and η. Higher η could reduce the ration of untraceable infectors either.

G: The relationship between the ration of untraceable infectors and the daily mean temperature.

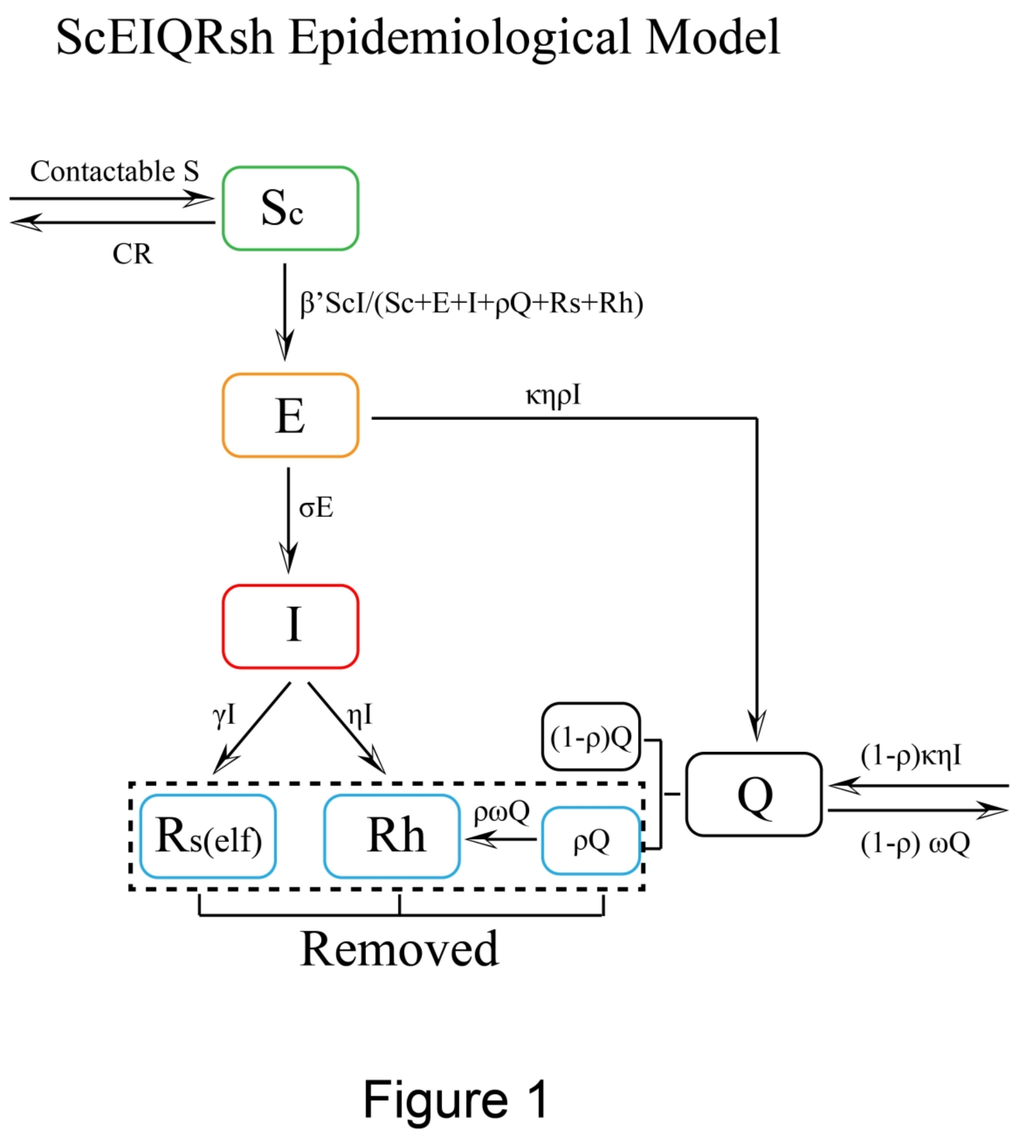

Figure 1

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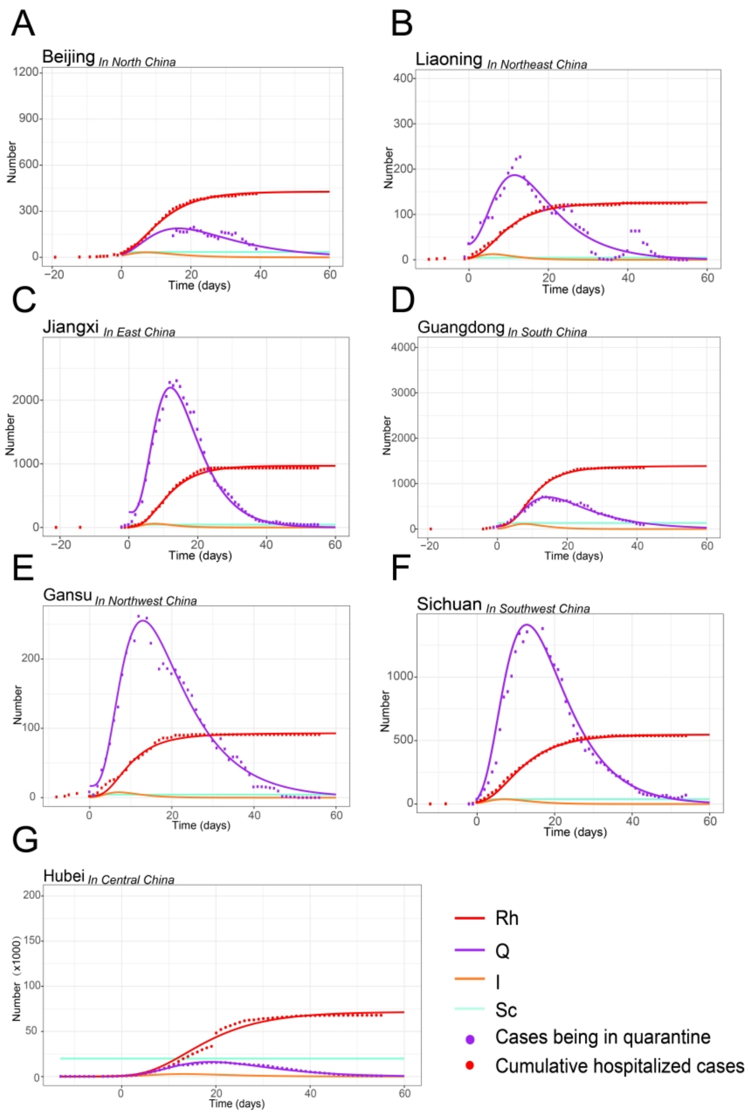

Figure 2

Figure 2

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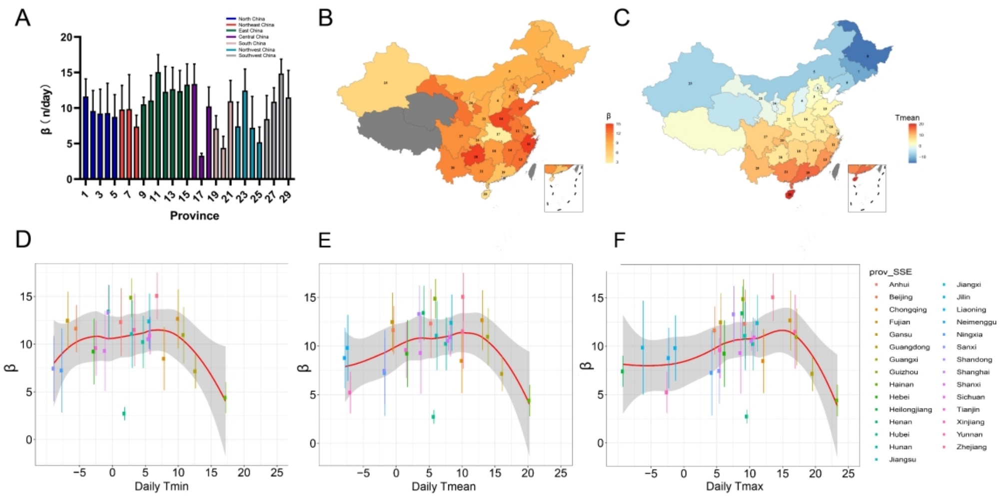

Figure 3

Figure 3

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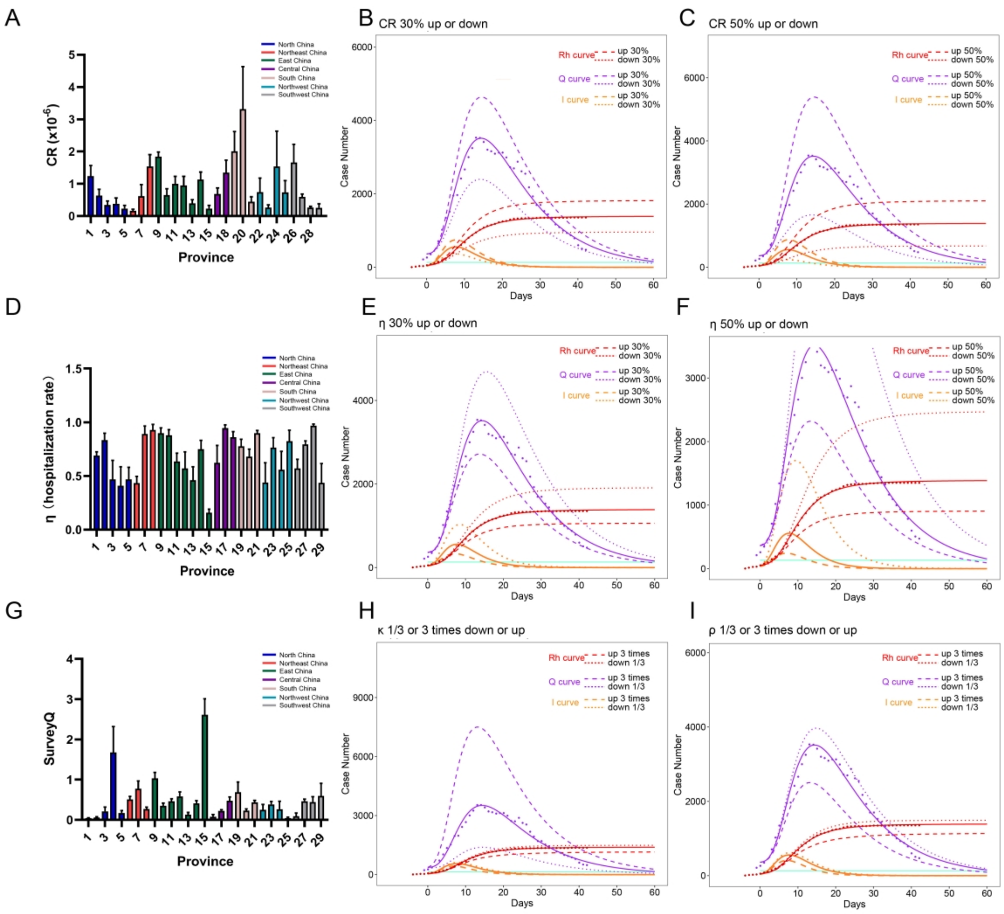

Figure 4

Figure 4

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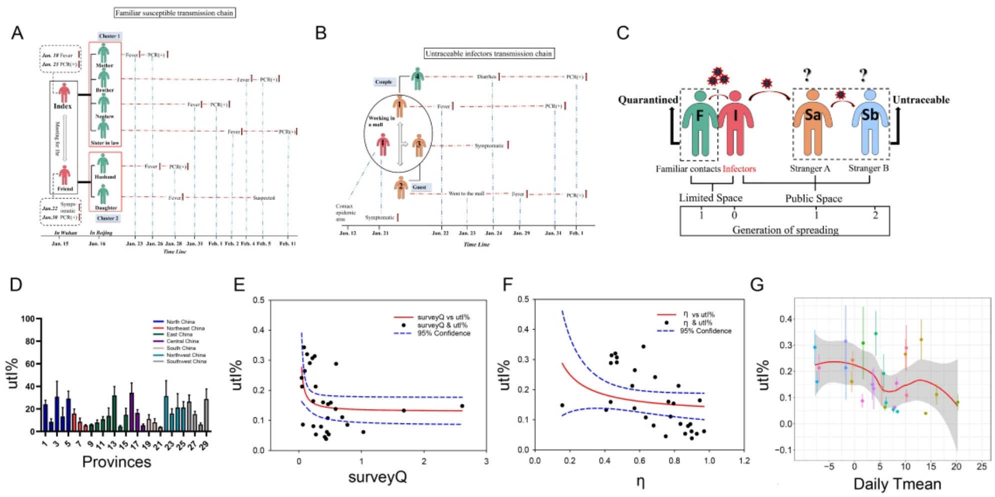

Figure 5

Figure 5

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The impact of air temperature and containment measures on mitigating the intra-household transmission of COVID-19: a novel data-based comprehensive modeling analysis

Di Liu [*,1], Qidong Tai [*,2], Yaping Wang [3], Miao Pu [3], Lei Zhang [†,2], Bo Su [†,1]

Supplementary methods

The stochastic ScEIQRsh epidemiological model

To simulate the epidemiological data of COVID-19 intra-household transmission under NPIs implementation, we developed an early spreading, early non-pharmaceutical-intervention stochastic model, denoted as ScEIQRsh model. The flow diagram of ScEIQRsh model was as the following, which demonstrated as following:

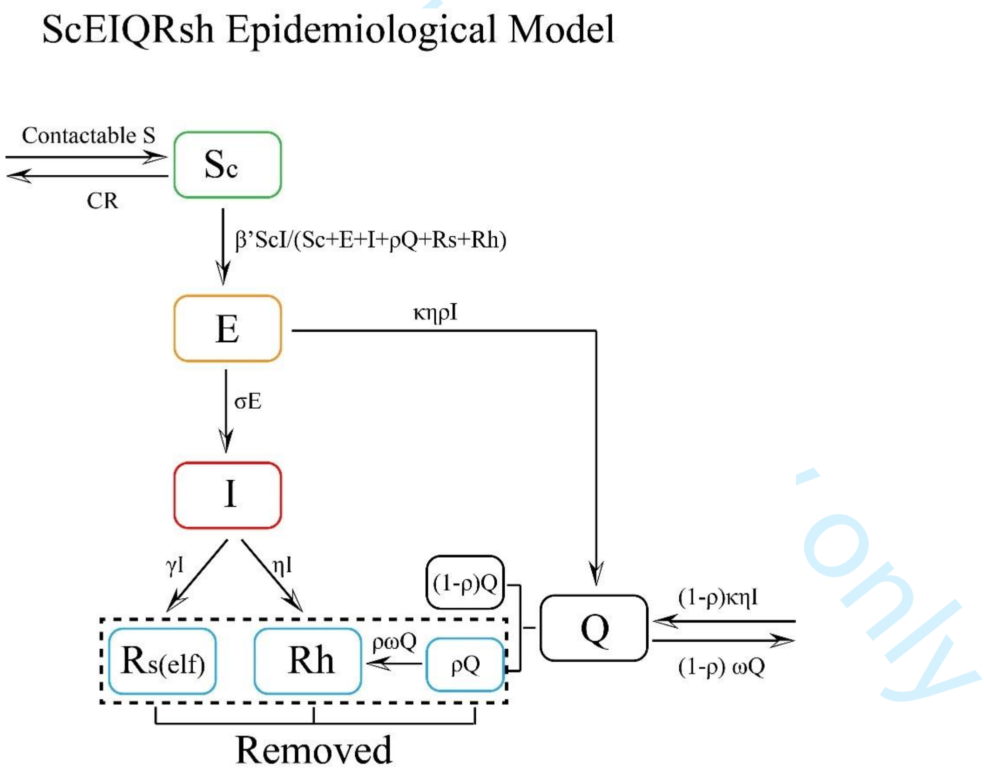


Figure 1

Compartments of the stochastic ScEIQRsh model

Sc: The contactable susceptible subpopulation for the infectors, comprised of their family, relatives, co-workers, friends, and some strangers who could be contacted by the infector under the interventive social prevention. The initial Sc is defined as a continuous random variable with Gaussian distribution in the model. The left arrow of Sc

means the susceptible could be entered into this compartment to become the contactable susceptible (just a part of the susceptible) at the rate of c.

E: The exposed individuals who are in the incubation period after effective contact with the infectors.

I: The infectors, either immigrant or local reproductive infectors who are still outsides of the public health measures.

Q: The close contacts of infectors found out by epidemiological survey, and notified to be in self-quarantine at home, in the hotel or indicated isolating room for 14-day medical observation. The Q value in this model is the daily reported cumulative close contacts or entry of medical observation minus the daily cumulative dismission of medical observation for each province. The right arrow of Q means the quarantined individuals who are not be diagnosed as infectious leave the compartment Q to be the susceptible again at the rate of $(1-\rho)\,\omega Q$, the opposite arrow means the susceptible in close contacts (in fact, only a small part of close contacts in contact tracing were infected, and the other were still the susceptible) enter the compartment Q at the rate of $(1-\rho)\kappa\eta I$.

Rs(elf): No all the infectious may see a doctor, especially the non-symptoms infectors. Some of the COVID-19 cases can be self-healing. Thus, the self-recovery individuals who have never be diagnosed and hospitalized because of mild symptoms, or asymptomatic infection, and thus were not be recorded in the daily official epidemic reports is designated as Rs.

Rh: The cumulative individuals who were etiologically diagnosed (mostly SARS-CoV-2 RNA rtPCR positive in oropharyngeal swabs, and inconsistent with other clinical symptoms) and hospitalized in isolate wards. The cumulative number includes any hospitalizing, or dead, or cured COVID-19 patients. In China, every confirmed case had been hospitalized in isolation wards, he/she cannot infect others, so can be regarded as removed.

Removed: The removed means any infectors who have been deprived of the ability to propagate, either by the gain of immunity (Rs, cured in Rh) or by public health measures (infectors in Q, the hospitalizing in Rh), or death (the dead in Rh). The removed in this model is the sum of cumulative Rs, Rh, and the positive cases in Q. So, the flow velocity to Rs and Rh was different.

Model validation

The value of parameters was randomly sampled with one of MCMC method, Metropolis-Hastings (M-H) algorithm, and documented under an appropriate tolerance of best fitting with at least 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for every province of Mainland China.

Other indexes

CR: restriction factor, the proportion of contactable susceptible (Sc) over the total population of a province under the interventive social prevention, which is simply calculated as Sc/N.

utI%: the proportion of the self-recovery removed, including asymptomatic infections or any infection without hospitalization and report, which were estimated as $\gamma/(\eta+\kappa\rho\eta+\gamma)$.

SurveyQ: an estimation for the quality of the epidemical survey, which is calculated as κ•ρ.

Incubation period: The incubation period was the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent, calculated with $1/\sigma+1/\eta$.

Communicable period: The time for untraceable infectors with contagious among susceptible, calculating with $1/\gamma$.

The air temperature of every province during the COVID-19 outbreak and spreading

The historical meteorological data were collected from china's meteorological administration. The daily mean air temperature was calculated from Jan 15, 2020 to Feb 15, 2020, i.e., from a week before Jan 23, 2020, to 3 weeks after that. In this period, COVID-19 began spreading and controlled by NPI in most of the provinces of China, except Hubei.

The epidemical data and epidemical survey of 31 provinces

The daily confirmed and quarantined cases were used for fitting the model. Almost all the diagnosed cases were hospitalized in isolation wards simultaneously according to the Guidance, thus the reported confirmed cases were just the hospitalized infectors in China. Cases confirmed with a laboratory test of the same sample identified two targets positive detection with real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assay or high-throughput sequencing, one is ORF, another one is the N protein of SARS-CoV-2. The quarantined cases were the population close contact the confirmed cases, asymptomatic infections, and suspected cases identified with epidemiological investigation within 24 hours. The close contacts were including:

1) living, studying, working in the same house with the confirmed or suspected cases.

2) medical staff, family members, or other persons who have close contact with cases in the process of diagnosis, treatment, or nursing.

3) take the same transport and have close contact with infectors, including caregivers, peers, or other passengers(*31*).

The quarantined people were isolated in the home or a specific place for observation of their symptoms for 14 days. If the lab testing results of close contacts of confirmed cases and asymptomatic infections are negative during the medical observation period, they still need to continue quarantine until the end of the observation of 14 days. Those who are in close contact with suspected cases can be relieved of medical observation when suspected cases are excluded from infection.

The provinces of China

There are 34 provincial-level administrative divisions of China, including 23 provinces, 4 municipalities (Beijing, Tianjin, Shanghai, Chongqing), 5 autonomous regions (Guangxi, Inner Mongolia, Tibet, Ningxia, Xinjiang) and 2 special administrative regions (Hong Kong, Macau). 23 provinces are including Anhui, Fujian, Gansu, Guangdong, Guizhou, Hainan, Hebei, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Liaoning, Qinghai, Shaanxi, Shandong, Shanxi, Sichuan, Yunnan, Zhejiang, Taiwan. Seven geographical regions were classified as Mainland

China, named as North China, Northeast China, East China, Central China, South China, Northwest China, Southwest China. The 29 provinces were included in our study, and they were separated into each geographical region and represented by numbers as follows:

1) North China: Beijing, Tianjin, Hebei, Shanxi, Inner Mongolia (1-5);

2) Northeast China: Liaoning, Jilin, Heilongjiang (6-8);

3) East China: Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong (9-15) and Taiwan;

4) Central China: Henan, Hubei, and Hunan (16-18);

5) South China: Guangdong, Hainan, Guangxi (19-21), Hongkong, and Macau;

6) Northwest China: Shaanxi, Gansu, Ningxia, Xinjiang (22-25) and Qinghai;

7) Southwest China: Chongqing, Sichuan, Guizhou, Yunnan (26-29), and Tibet.

Supplementary tables

Table S1. The mean value of parameters and indexes in each province of Mainland China

	Parameters and indexes (Mean±SD)										
Province	**β'**	**σ**	**γ**	**η**	**κ**	**ρ(%)**	**ω**	**CR**	**Ipd (day)**	**utI%**	**Survey Q**
All provinces	10.01±2.86	0.42±0.04	0.16±0.07	0.68±0.20	45.55±28.66	1.32±1.30	0.12±0.03	1.58E-05±7.88E-05	4.31±1.18	15.63±9.27	0.46±0.53
Beijing	11.63±2.48	0.35±0.02	0.23±0.05	0.69±0.04	5.59±0.17	0.78±0.12	0.07±0	1.24E-06±3.24E-07	4.34±0.19	24.22±3.57	0.04±0.01
Tianjin	9.58±2.89	0.33±0.03	0.08±0.03	0.83±0.06	12.79±0.72	0.49±0.12	0.07±0	6.35E-07±1.95E-07	3.71±0.3	8.7±2.58	0.06±0.02
Hebei	9.22±3.44	0.41±0.06	0.22±0.06	0.47±0.18	46.56±6.34	0.47±0.24	0.16±0.02	3.38E-07±1.27E-07	5.05±1.07	30.75±13.89	0.22±0.11
Shanxi	9.29±4.2	0.41±0.05	0.14±0.07	0.41±0.18	65.78±15.26	2.49±0.57	0.14±0.02	3.77E-07±1.82E-07	3.89±1.29	13.35±7.9	1.68±0.64
Neimenggu	8.77±3.12	0.44±0.03	0.22±0.04	0.47±0.11	62.99±5.38	0.27±0.08	0.15±0.01	2.34E-07±9.11E-08	4.55±0.59	29.11±6.61	0.17±0.06
Liaoning	9.81±3.38	0.48±0.02	0.13±0.04	0.43±0.06	27.96±1.68	1.82±0.27	0.12±0.01	1.64E-07±5.09E-08	4.46±0.35	15.98±4.01	0.51±0.08
Jilin	9.85±4.85	0.41±0.06	0.15±0.06	0.89±0.07	58.58±14.51	1.35±0.28	0.13±0.03	6.15E-07±3.60E-07	3.6±0.38	8.62±3.27	0.77±0.2
Heilongjiang	7.39±1.62	0.44±0.03	0.07±0.01	0.93±0.05	27.83±1.98	0.98±0.16	0.11±0.01	1.53E-06±3.76E-07	3.35±0.19	5.43±0.73	0.27±0.05
Shanghai	10.53±1.01	0.41±0.07	0.12±0.01	0.9±0.05	64.41±2.25	1.6±0.19	0.21±0.02	1.84E-06±1.44E-07	5.44±0.54	6.22±0.42	1.03±0.15
Jiangsu	11.06±3.55	0.44±0.04	0.1±0.03	0.88±0.05	32.43±3.1	1.08±0.12	0.15±0.01	6.53E-07±1.96E-07	3.45±0.24	8.01±2.27	0.35±0.06
Zhejiang	15.06±2.46	0.48±0.02	0.11±0.03	0.64±0.08	34.64±2.55	1.33±0.16	0.1±0.01	1.00E-06±2.37E-07	3.67±0.24	10.83±2.35	0.46±0.06
Anhui	12.31±3.55	0.38±0.03	0.14±0.07	0.57±0.15	36.65±4.4	1.61±0.29	0.13±0.01	9.51E-07±2.86E-07	4.55±0.55	13.88±7.03	0.59±0.11

Fujian	12.66±3.09	0.45±0.03	0.23±0.04	0.46±0.12	42.01±2.93	0.31±0.14	0.13±0.01	3.89E-07±1.17E-07	4.55±0.61	32.08±7.71	0.13±0.06
Jiangxi	12.38±2.91	0.41±0.03	0.05±0.01	0.75±0.08	48.15±2.52	0.86±0.11	0.16±0.01	1.13E-06±2.36E-07	3.81±0.18	4.59±0.8	0.41±0.07
Shandong	13.3±2.94	0.35±0.06	0.1±0.06	0.16±0.03	51.26±3.2	5.09±0.69	0.08±0.01	2.36E-07±9.04E-08	9.62±1.3	14.88±5.82	2.61±0.4
Henan	13.4±2.8	0.45±0.03	0.26±0.03	0.62±0.16	24.87±2.71	0.31±0.18	0.12±0.01	6.84E-07±1.90E-07	4.56±0.95	34.36±8.6	0.08±0.05
Hubei	3.29±0.34	0.42±0.05	0.23±0.04	0.95±0.03	5.35±0.62	4.28±0.48	0.11±0.01	4.33E-04±8.35E-05	3.48±0.29	16.49±2.9	0.23±0.03
Hunan	10.22±2.73	0.45±0.03	0.07±0.01	0.86±0.05	38.98±2.47	1.22±0.2	0.16±0.01	1.35E-06±3.82E-07	3.42±0.19	5.44±1.2	0.48±0.09
Guangdong	7.14±1.79	0.44±0.04	0.16±0.06	0.78±0.06	14.33±1.33	4.87±1.82	0.17±0.02	2.01E-06±6.07E-07	3.58±0.26	11.14±3.78	0.69±0.25
Hainan	4.39±1.63	0.44±0.04	0.07±0.03	0.68±0.07	23.03±1.83	1±0.18	0.08±0.01	3.32E-06±1.31E-06	3.78±0.25	8.17±3.17	0.23±0.05
Guangxi	10.95±2.94	0.46±0.02	0.05±0	0.9±0.03	52.88±2.53	0.82±0.08	0.11±0	4.45E-07±1.51E-07	3.27±0.13	3.92±0.3	0.43±0.05
Shaanxi	7.44±3.41	0.4±0.05	0.22±0.05	0.44±0.18	76.13±8.4	0.33±0.17	0.1±0.01	7.43E-07±4.38E-07	5.52±1.91	31.44±13.72	0.25±0.13
Gansu	12.46±3.04	0.45±0.03	0.2±0.05	0.76±0.09	41.99±3.6	0.92±0.14	0.1±0.01	2.66E-07±7.72E-08	3.56±0.27	16.08±4.02	0.39±0.07
Ningxia	7.24±4.41	0.36±0.06	0.17±0.07	0.56±0.17	70.9±11.44	0.37±0.26	0.11±0.02	1.53E-06±1.10E-06	4.91±1.29	21.31±12.15	0.27±0.19
Xinjiang	5.21±2.13	0.41±0.05	0.23±0.05	0.82±0.1	147.79±11.06	0.03±0.01	0.08±0	7.34E-07±3.67E-07	3.71±0.32	21.32±5.08	0.05±0.02
Chongqing	8.47±3.31	0.42±0.03	0.22±0.04	0.57±0.08	39.36±6.01	0.22±0.16	0.13±0.01	1.66E-06±5.67E-07	4.17±0.34	26.52±5.82	0.09±0.08
Sichuan	10.9±1.96	0.38±0.03	0.21±0.04	0.79±0.03	46.84±3.25	0.99±0.07	0.12±0.01	5.92E-07±9.07E-08	3.89±0.22	15.47±2.48	0.47±0.05
Guizhou	14.87±2.03	0.35±0.03	0.09±0.02	0.97±0.02	23.7±3.5	1.86±0.37	0.17±0.02	2.63E-07±3.44E-08	3.92±0.25	6.25±1.45	0.45±0.13
Yunnan	11.49±3.82	0.44±0.04	0.25±0.04	0.44±0.18	97.33±33.65	0.59±0.19	0.15±0.04	2.60E-07±1.18E-07	5.14±1.62	28.89±8.82	0.59±0.31

Abbreviation: Ipd: Incubation period; utI%: Proportion of Untraceable infectors;

Supplementary figure legend

Figure S1. The fitting curves of both the number of daily cumulative confirmed cases and close contacts being in quarantine in 22 provinces of Mainland China (Day 0, the 23rd, Jan, 2020).

A: The fitting curve of provinces in Northwest China- Xinjiang/ Shaanxi/ Ningxia and Central China-Hunan/ Henan.

B: The fitting curve of provinces in South China- Hainan/ Guangxi, and Southwest China-Yunnan/ Guizhou/ Chongqing.

C: The fitting curve of provinces in East China- Shanghai/ Zhejiang/ Anhui/ Fujian/ Shandong/ Jiangsu.

D: The fitting curve of provinces in North China- Neimenggu/ Tianjin/ Hebei/ Shanxi and Northeast China-Heilongjiang/ Jilin.

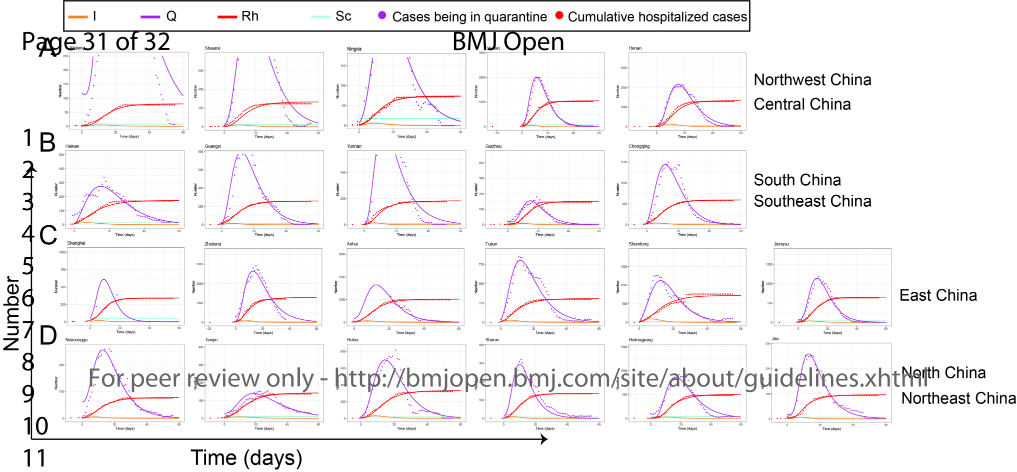
Figure S2. Suppositional simulation of contact tracing parameters, κ and ρ.

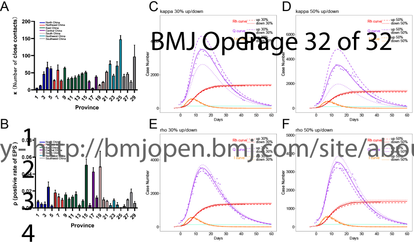
A-B: The median κ and ρ was observed as different among 29 provinces.

C-D: The influence on Rh, Q and I compartment after adjustment of κ by 30% or 50%.

E-F: The simulated Rh, Q and I compartment after adjustment of ρ by 30% or 50%.

Figure S3. The median incubation period of COVID-19 among 29 provinces.


I
Q
Rh
Sc
Cases being in quarantine
Cumulative hospitalized cases
A
Xinjiang
Shaanxi
Ningxia
Hunan
Henan
Northwest China
Central China
B
Hainan
Guangxi
Yunnan
Guizhou
Chongqing
South China
Southeast China
C
Shanghai
Zhejiang
Anhui
Fujian
Shandong
Jiangsu
East China
D
Neimenggu
Tianjin
Hebei
Shanxi
Heilongjiang
Jilin
North China
Northeast China
Number
Time (days)


A
κ (Number of close contacts)
North China
Northeast China
East China
Central China
South China
Northwest China
Southwest China
Province
B
ρ (postive rate of EPS)
Province
C
kappa 30% up/down
Rh curve
Q curve
up 30%
down 30%
Case Number
Days
D
kappa 50% up/down
up 50%
down 50%
E
rho 30% up/down
F
rho 50% up/down
T curve

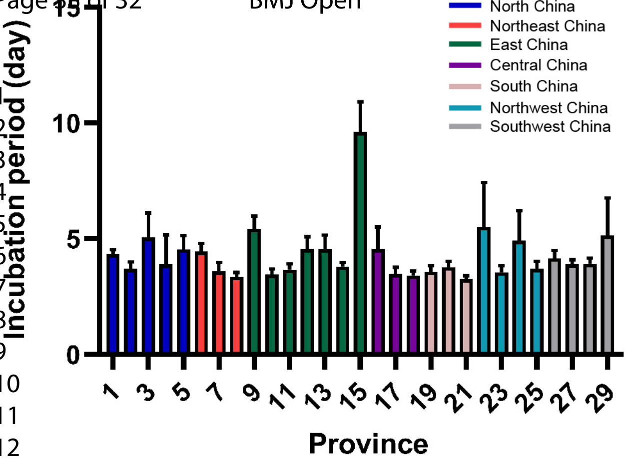

Incubation period (day)
15
10
5
0
North China
Northeast China
East China
Central China
South China
Northwest China
Southwest China
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29
Province

Figure S3

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The impact of air temperature and containment measures on mitigating the intra-household transmission of SARS-CoV-2: a data-based modeling analysis

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The impact of air temperature and containment measures on mitigating the intra-household transmission of SARS-CoV-2: a data-based modeling analysis

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Running Head: Air temperature impacting COVID-19 control

Keywords: COVID-19; air temperature; non-pharmaceutical Interventions; mathematical model; asymptomatic

Abstract

Objectives

Air temperature has been considered as a changeable and contributable variable in coronavirus disease 2019 (COVID-19) transmission. And, the implementation of non-pharmaceutical interventions (NPIs) also made an impact to COVID-19 transmission, changing the transmission pattern to intra-household transmission under stringent containment measures. Therefore, it is necessary to re-estimate the influence of air temperature on the COVID-19 transmission while excluding the NPIs' influence.

Design, setting and participates

This study used a data-based comprehensive modeling analysis. A stochastic epidemiological model (contactable Susceptible-Exposed-Infected-Removed model (ScEIQR)) was established to evaluate the influence of air temperature and containment measures on the intra-household spreading of COVID-19. The epidemic data of COVID-19, including daily confirmed cases and the number of close contacts, etc., was collected from the National Health Commission of China.

Outcome measures

The model was fitted using Metropolis-Hastings (M-H) algorithm with a cost function based on the least-squares method. The LOESS regression function was used to assess the relationship between air temperature and COVID-19 transmission rate within the ScEIQR model.

Results

The ScEIQR model indicated that the optimal temperature for COVID-19 spreading peaked at 10℃ (50°F), ranging from 5℃ to 14℃ (41°F-57.2°F). In the fitted model, the fitted intra-household transmission rate (β') of COVID-19 was 10.22 (IQR 8.47, 12.35) across mainland China. The association between air temperature and the β' of COVID-19 suggested that the COVID-19 pandemic might be seasonal. Our model also validated the effectiveness of NPIs, demonstrating that diminishing contactable susceptibility (Sc) and avoiding delay in diagnosis and hospitalization (η) were more effective than contact tracing (κ, ρ).

Conclusions

We constructed a novel epidemic model to estimate the effect of air temperature on COVID-19 transmission beyond NPIs' implementation, which can inform the public health strategy and predict the transmission of COVID-19.

Strengths and limitations of this study

- We used a Metropolis-Hastings (M-H) algorithm, a Markov Chain Monte Carlo (MCMC) method, to establish a novel epidemiological contactable Susceptible-Exposed-Infected-Removed model (ScEIQR).
- The stochastic ScEIQR model can fit well the early spreading and early social intervention data of COVID-19.
- The study explored the influence of air temperature on COVID-19's intra-household transmission.
- The limited latitude span in this study narrowed the range of the explored air temperature.

Introduction

The COVID-19 has been spreading for more than two years in many countries. Many factors, such as the virus virulence, the host defense potential, and the number of contacts *overall* could affect the transmission[1]. Since the influenza virus is affected by the changes in temperature and relative humidity, the air temperature might be an important factor for influencing the transmission of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which caused the COVID-19 epidemic[2]. However, the effects of the meteorological indicators on COVID-19 transmission are unclear. A few studies have reported that air temperature influences the COVID-19 pandemic. Bilal and colleagues found a significant association between the temperature and the COVID-19 pandemic in the USA[3 4] and Germany[5]. However, some researchers have reported a contradictory finding[6 7]. Thus, the effect of air temperature on COVID-19 transmission remains controversial.

In the past two years, governments of many countries implemented several non-pharmaceutical interventions (NPIs), including physical and social distancing, quarantine, and isolation to mitigate the COVID-19 outbreak in the early stage[8]. In China, the COVID-19 pandemic diminished within two months as direct result of NPIs executed since Jan 23, 2020. Besides increasing physical and social distance, contact tracing and hospitalized isolation were applied [9]. These containment measures were effective for controlling the spread of COVID-19.

However, what's the influence of air temperature on the COVID-19 incidence and transmission rate beyond NPIs' effect?

We then used the data from China as an appropriate example to evaluate the relationship between the air temperature and the spread of COVID-19. First, the social intervention in China was taken almost simultaneously and uniformly across provinces, differing only in intensity. Second, the latitude span of mainland China is large enough to reflect the zones with a daily mean air temperature of -7℃ to 20℃ in winter. Third, we could get the complete data of the daily numbers of cases in quarantine by contact tracing in each province. Thus, we constructed a new kind of SEIR (Susceptible-Exposed-Infected-Removed) model, called ScEIQR (contactable Susceptible-Exposed-Infected-Quarantined-Removed) to depict a new spreading pattern of COVID-19, the intra-household transmission. The model can separate the influence of social intervention measures from confounding factors. Hence, with machine learning methods, we achieved the precise influence of air temperature on COVID-19 spreading. Moreover, this model validated the effectiveness of the NPIs in controlling the COVID-19 transmission.

Materials and Methods

Development of the dynamical non-classical SEIR model for COVID-19

The developed ScEIQR model is an expanded SEIR epidemic model containing six compartments, Sc (contactable susceptible), E (the exposed to SARS-COV-2), Q (daily close contacts being in quarantine), I (infectors outside of the healthcare system), Rh (accumulative hospitalized infectors), and Rs (self-recovery individuals with asymptomatic infection or mild symptoms who have never be hospitalized and registered in healthcare system) (Figure 1). Sc represents the contactable susceptible social NPIs, such as lockdown, social distancing, canceling gatherings, and closing public places, which were set as a random variable in the model. Q represents the close contact tracing (CCT) for quarantine, Rh represents the confirmed and hospitalized infectors in isolation wards, reported daily by public health agency. E, I, and Rs compartments were outside of the healthcare system. Rh was the reported cumulative confirmed cases in the model. Several parameters linked the compartments, , and the flow velocity of each compartment is illustrated in Figure 1 (details in the supplementary methods).

Parameters of the stochastic ScEIQR model

The definition and initial range of model parameters of β', σ, γ, κ, ρ, ω, η and Sc in the model were listed in Table 1. β' was the intra-household transmission rate dependent on the property of SARS-COV-2. σ and γ were associated with the intrinsic incubation period and communicable period of COVID-19. κ, ρ and ω were associated with contact tracing and quarantine. η reflected the pace of confirmed diagnosis and hospitalized isolation for infectors. Other indexes could be calculated from the solved model, such as the contact rate (CR), the quality of CCT (surveyQ), the proportion of untraceable infectors (approximately equate to the asymptomatic) (utI%), the incubation period and communicable period of SARS-COV-2, and among them, CR reflects the proportion of Sc in population under the integrated NPIs, surveyQ represents the quality of contact tracing.

β': the effective intra-household transmission rate for the contactable susceptible (Sc).

σ: the progression rate from exposed to being infectious, which is the reciprocal of the incubation period (days) in the propagate chain.

γ: the removal rate for Rself, which is the reciprocal of the apparent period of being propagating for a self-recovery infector in the propagate chain.

η: the removal rate for Rh, which is the reciprocal of the apparent period of being propagating for a hospitalized infector in the propagate chain.

κ: the average number of traceable close contacts for each confirmed case, which was investigated and notified to be in quarantine by the epidemiological survey group of each province. All the found close contacts were assumed to be in a 14-day quarantine.

ρ: the virus-positive rate of the individuals in quarantine for each province.

ω: the dismiss rate of virus-negative individuals in quarantine

Formulation and Parameters setting of ScEIQRsh model

The simultaneous differential equations system for the stochastic ScEIQRsh model is as follows:

(1) $dE/dt = \beta' ScI/(Sc+E+I+Rs+Rh+\rho Q) - \kappa\eta\rho I - \sigma E$;

(2) $dI/dt = \sigma E - \eta I - \gamma I$;

(3) $dQ/dt = \kappa\eta I - \omega Q$;

(4) $dRh/dt = \eta I + \rho\omega Q$;

(5) $dRs/dt = \gamma I$;

* In equation (1), unlike the classical SIR or SEIR model, the denominator of flow-in velocity is ($Sc+E+I+Rs+Rh+\rho Q$) instead of N or any other constants. The denominator means all the transmitted individuals in the system. The classical SIR or SEIR model assumes that the infectors mix up with different susceptible every day, and ScEIQR model assumes that the infectors mix up with the fixed contactable susceptible every day.

The parameters setting: β', σ, γ and η were set as random variables with Gaussian distribution; κ, ω, ρ was set as random variables with uniform distribution. Parameters range setting: β' [1,19], σ [0.27,0.5], γ [0.04,0.3], η [0.001,0.999], κ [0,350], ω [0.07,0.6], ρ [0,0.1].

Sc was set as a random variable with Gaussian distribution and the range setting was Sc(0,0.002N]. N denotes the total population of the province. The other initial compartment values were estimated as the following: initial Rh=H0, initial Rs=0, initial Q=Q0, initial I=H0*(1-η)/η, initial E= initial I/σ. H0, Q0 denotes the cumulative hospitalized cases, close contacts in quarantine at Day 0 (23rd, Feb 2020) reported by the public health administration of the province. If H0 or Q0 is missing for some province, H0 or Q0 will be given an assumed number.

Epidemic data acquisition

The intra-household transmission of COVID-19 [10] were observed from the beginning of COVID-19 in mainland China [11]. Each Provincial Health Commission would report the daily number of close contacts being in quarantine along with the number of daily confirmed cases of COVID-19. This complete data from mainland China were appropriate for fitting the ScEIQR model and investigating the intra-household transmission of COVID-19. We collected the data of daily accumulative confirmed COVID-19 cases from January to March, 2020 from the provincial health commission of mainland China. The daily number of close contacts in quarantine and the daily number of those relieved of quarantine were also collected from the provincial government website in China. The Xizang and Qinghai provinces were excluded because they had only one and 18 confirmed cases, respectively. According to the COVID-19 guidelines of China, the diagnosed cases of COVID-19 were hospitalized in isolation wards; thus, the reported confirmed cases were the hospitalized infectors in China. Details about the quarantine criteria for confirmed cases and close contacts are clarified in the supplementary methods.

Simulation and model fitting

We fitted both the reported accumulative confirmed cases and daily close contacts of each province with Rh and Q compartments in ScEIQR model by Markov Chain Monte Carlo (MCMC) method with a cost function based on least-squares method. Briefly, model parameters and Sc were random samplings with Metropolis-Hastings (M-H) algorithm, aMarkov Chain Monte Carlo (MCMC) method. The proposal distribution for accept-reject is a Bernoulli distribution from the comparison of the cost function of curve fitting in iteration (better or not). Both simulated curves of Rh and Q were simultaneously fitted with the raw data (the real word data) by the least-squares method. And the cost function was SSE/SST (Sum of Squares for Error/Sum of Squares for Total). The optimized parameters were documented with 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for 29 provinces of mainland China. The expected value and standard deviation for each parameter were then confirmed.

Air temperature of provinces in China during the COVID-19 spread

The minimum (Tmin), mean (Tmean), maximum (Tmax) air temperatures for each province were collected from the National Meteorological Administration from Jan 15, 2020, to Feb 15, 2020 (one week before and three weeks after Day 0), which was Jan 23, 2020. The LOESS regression depicted the relationship between the air temperature in 29 provinces and the COVID-19 transmission rate in the ScEIQR model.

Patient and Public Involvement

No patient was involved.

Statistical analysis

The enrolled 29 provinces were separated into seven geographical regions: North, Northeast, East, Central, Northwest, South and Southwest China. The curves of Rh and Q were simultaneously fitted with the raw data using the least-squares method with a tolerance of 1.05. SSE/SST (Sum of Squares for Error/Sum of Squares for Total) as the cost function. The data process was performed in R (version 3.6.1), and the “deSolve” R package was used as the solver of differential equations. The R source code can be found in *GitHub*. The parameters were denoted as mean±SD for each province, and the median (interquartile range, IQR: 25%, 75%) was used to describe provinces.

Results

The influence of air temperature on the transmissibility of COVID-19

The intra-household transmission rate (β') was calculated first, and subsequently, the nonlinear association between β' and the air temperature was depicted by LOESS fitting.

The intra-household transmission rate (β') calculated

First, we fit the COVID-19 transmission with integrated social NPIs using the ScEIQR model, which could be well fitted with the reported number of daily accumulative confirmed cases and close contacts in quarantine in 29 provinces of mainland China (Figure 2, Figure S1). The predicted daily Rh and Q compartments coincided with the provincial reported numbers. The fitting curves, yielded the median intra-household transmission rate (β') for 29 provinces were 10.22 (IQR 8.47, 12.35), implying that 10.22 person would be infected by one infector when the susceptible are mostly acquaintances and Sc is extrapolated to infinite (Figure 3A-B, Table 2, Table S1).

The range of air temperature for COVID-19 spread

The mean air temperature for every province in China was spanned from -15 ℃ (5 °F) to 20.25 ℃ (68.45 °F) between Jan and Feb 2020 in China (Figure 3C). The relationship between the air temperature and β' was evaluated. As the daily air temperature increased from zero (0℃, 32°F), the value of β' raised gradually until the air temperature reached 7℃ (44.6°F) for a minimum daily temperature, or 15℃ (59°F) for a maximum daily temperature, respectively, and then declined sharply as the temperature continued to rise (Figure 3). We observed that the transmission rate (β') was higher than 11 for mean air temperature in the 5℃-14℃ (41°F-57.2°F), which may be most suitable for COVID-19 spread.

Validation the NPIs on mitigating the COVID-19 spread

The COVID-19 pandemic hit many countries because of the coronavirus mutation. Therefore, the containment measures are still pivotal for controlling COVID-19 spread.

Assessment of NPI measures by suppositional simulation

We assessed three independent parameters, contact rate (CR), η and surveyQ, which were crucial for stopping the spread. Our model estimated the median Sc of 26.98 (IQR:13.97, 54.57), with the highest value in Hubei and lowest in Neimenggu province (Table S1). The median CR for 29 provinces was 6.84E-07 (IQR 3.77E-07, 1.44E-06) (Figure 4A). To illustrate the influence of NPI measures on COVID-19 transmission in the ScEIQR model, we arbitrarily adjusted CR, κ, ρ, and η values with representative 30% or 50% up/down-regulation to simulate the suppositional spreading situation. If CR were 30% or 50% enlarged, the eventual accumulative hospitalized cases (Rh) would strongly increase, the infectors (I) would be reduced and vice versa (Figure 4B, 4C). The median for the velocity of hospitalized isolation of infectors (η) was 0.69 (IQR 0.47, 0.87) for 29 provinces (Figure 4D). The influence of η on CR was the opposite. If the η increased by 30% or 50%, the eventual Rh would be strongly reduced and vice versa (Figure 4E, 4F).

SurveyQ, the product of κ times ρ, was 0.39 (IQR 0.22, 0.55), which indicated that on average, 0.39 of positive cases were in close contact with confirmed infectious individuals according to CCT (Figure 4G). The κ and ρ can be used to assess the effectiveness of CCT, and the median κ of 29 provinces was 42.0 (IQR 27.83, 60.78), suggesting that, on average, 42 close contacts of a infector had been traced by CCT (Figure S2A). The COVID-19 positive rate (ρ) among close contacts was 0.98% (IQR 0.47%-1.60%), ranging from 0.03%-5.10% (Figure S2B), which was quite close to the WHO-China joint report of 0.9%-5% in China [11]. With higher κ or ρ, the eventual accumulative number of confirmed COVID-19 would diminish, and the Rh reach a plateau (Figure 4H, 4I, Figure S2C, D, E, F). For the same adjusted extent, the effectiveness of CR and η on spread prevention was stronger than that of CCT parameters, κ and ρ. The incubation period and communicable period of COVID-19 were calculated using the ScEIQR model, and the results were consistent with other studies (Table 2, Figure S3), suggesting that this novel model is reasonable.

Blind zone of contact tracing and asymptomatic infectors in NPIs

With the integrated social NPIs, COVID-19 transmission occurred between undetected infectors and acquaintances, and a few strangers whom the infectors had to contact for daily necessities. In a typical intra-household transmission, the index case infected directly four family members and one friend, and indirectly the friend's family within half a month[12] (Figure 5A). CCT can easily find close contacts of acquaintances but be inefficient in finding transmission among strangers in public space. For example, a salesman infected two unacquainted sales associates in other sales areas sequentially without gathering in a large mall, and one of the infected sales associates transmitted the infection to a customer without direct contact after 30-minutes lingering (Figure 5B). This transmission chain in strangers could not be easily found by contact tracing and was only revealed after all the participants' symptoms appeared (Figure 5C).

Another blind spot of contact tracing is asymptomatic infection. The ScEIQR model showed that the proportion of asymptomatic and mild-symptom infectors without hospitalization (the proportion of untraceable infectors, utI%) was 14.88% (IQR 8.17%, 25.37%), ranging from 3.92%-34.36% across 29 provinces, which implied that 14.88% of COVID-19 patients, on average, could not be found with social NPIs, and the average proportion of asymptomatic COVID-19 patients was 14.88% (IQR 8.17%, 25.37%) (Figure 5D). The higher surveyQ of CCT can only reduce but not eliminate utI% (Figure 5E), but high η could decline the utI% (Figure 5F). Hence, contact tracing is insufficient to find all the infectors, especially in stranger-stranger transmission and asymptomatic infection. The air temperature also influences the ratio of asymptomatic infectors. When the mean air temperature was subzero, the utI% was high (Figure 5G).

Discussion

It is important to understand the effects of the meteorological conditions on the spread of COVID-19 to predictCOVID-19 prevalence, especially intra-household transmission. In our study, we found the transmission rate (β') increased as the air temperature rose from -5℃ (23°F), and the peak of β' appeared at the minimum, average, and maximum temperature of 7℃ (44.6°F), 10℃ (50°F), and 15℃ (59°F), respectively, and then started to decline at higher temperature across the 29 provinces in China. The finding is consistent with the curves reported by Wang Mao *et al.*[13], who have claimed that the peak of accumulative cases of 492 cities appeared at the minimum, average, and maximum temperature of 6.7℃ (44.06°F), 8.72℃ (47.7°F), and 12.42℃ (54.36°F), respectively. Wang Mao *et al.* [13] and Sajadi MM *et al.* [14] found that regions along the 30-50° N' latitude with an average temperature of 5℃-11℃ (41°F-51.8°F) had increased COVID-19 transmission. We also coincidentally discovered the optimal mean temperature ranges for COVID-19 transmission were 5℃-14℃ (41°F-57.2°F). Lowen *etal.* proved that influenza virus transmission by droplets was greater and the peak duration of virus shedding lasted longer at 5°C (41°F) than 20℃ (68°F)[15]. Indeed, the β' of COVID-19 at 5℃ (7.39±1.62) was higher than β' at

20.25℃ (4.39±1.63). Another similar infectious disease, SARS, was found to have a higher transmission rate in temperatures below 24.6℃ in Hong Kong [16]. From the curve we illustrated, we could suspect the transmission rate would be further reduced although not eliminated at temperatures greater than 20.25℃ (68.45 °F). It can be expected that COVID-19 pandemic spread would be moderate in northern hemispheres in the summer, and it is likely to become a seasonal infectious disease. The broader air temperature range for optimal COVID-19 transmission strongly suggests the current necessity and urgency of the vaccine.

Besides air temperature, the most important measures to contain the COVID-19 epidemic are the vaccine and the NPIs. After the first-level public health emergency response on Jan 23, 2020, integrated NPIs were implemented in Mainland China during COVID-19 epidemic [9]. The spread pattern of COVID-19 changed into the intra-household transmission. A report of the "WHO-China Joint Mission on COVID-19" verified that, about 78%-85% of infections in Guangdong and Sichuan province occurred within families [11]. In Beijing, 176 out of 262 confirmed cases were intra-household members[10]. Using our ScEIQR epidemic model, we estimated the effectiveness of integrated NPIs to simulate COVID-19 restricted spread among acquaintances for the first time. ScEIQR model can fit the realistic provincial epidemic and NPI data of COVID-19 in China without adjusting the parameters. Unlike the classical SEIR (Susceptible-Exposed-Infected-Removed) epidemic model, which assumes that infectors mix with all susceptible daily, the infectors in the ScEIQR model mix with the contactable susceptible daily, which indicates the family members, relatives, co-workers, friends, and some contactable strangers who deliver daily necessities to the infectors. Because the contact among acquaintances is more frequent than the contact among the whole population, the β' value tends to be larger in our model than in the classical SEIR model in other studies [17].

In the NPIs measures, CR and η are more effective in diminishing the eventual accumulative number of COVID-19 cases than CCT parameters κ and ρ. In case of insufficient medical resources, the better way to improve η could be to enlarge the laboratory capacity for SARS-COV-2 testing or build makeshift hospitals to increase bed capacity [18]. Contact tracing is also helpful for mitigating COVID-19 spread, especially among close contacts (quarantine for targeted susceptible) than among the common susceptible. The surveyQ (κ•ρ) of CCT could be improved by adding more CCT staff, loosening the criteria of close contacts in CCT, broadening SARS-COV-2 testing to close contacts, or using digital tools. It is undeniable that the above methods require more human and financial resources, and may not be suitable for every country.

Nevertheless, lockdown and stay-at-home orders profoundly affect society and the economy. Contact tracing is a less severe option without unnecessary quarantine. In brief, decreasing the number of the contactable susceptible (Sc or c) in individuals and increasing η are crucial factors for COVID-19 control.

Additionally, the asymptomatic but infectious individuals are the source for recurrence of the COVID-19 epidemic. We demonstrated that the median and the highest proportion of asymptomatic infectious people were 14.88% and 34.36%, respectively, consistent with the reported 18% among 700 infectious individuals who never showed symptoms on *Diamond Princess* by Kenji Mizumoto *et al.* [19] and 30.8% of asymptomatic cases in 565 Japanese citizens evacuated from Wuhan Hiroshi Nishiura *et al.* [20]. The low air temperature could also increase the proportion of asymptomatic infectors. Hence, it is crucial to implement containment measures in addition to monitoringthe air temperature. The incubation period that emerged from ScEIQR model is aligned with the 3 day incubation reported in a study of 1,099 laboratory-confirmed cases by Zhong *et al.*[21], which indicates that the model simulates the real-word transmission process accurately.

Our study was based on a novel ScEIQR NPIs model and only included the epidemic data from mainland China to validate the model because we could not access the NPIs data, e.g., close contacts in other countries. This model could be fitted even with limited NPIs data, although the results might be less accurate. The limited latitude spans in this study narrowed the range of air temperature, especially higher temperature; therefore, the association of air temperature with COVID-19 transmission rate was informative and suggestive[22].

Conclusions

In conclusion, we provide a new tool for quantitatively assessing the influence of air temperature or the effectiveness of NPIs strategy on the COVID-19 outbreak. We also speculated that the appropriate temperature for SARS-COV-2 transmission is within 5℃-14℃ (41°F-57.2°F) under the implementation of NPIs. The stochastic ScEIQR model was constructed, which can fit well the early spread and early social intervention data of COVID-19. The effectiveness of NPIs in mitigating the transmission of COVID-19 was evaluated. Keeping the contactable susceptible at a low level and promoting the prompt diagnosis and hospitalized isolation of COVID-19 positive individuals can mitigate early intra-household transmission of COVID-19, guiding the implementation of effective public health intervention strategy for COVID-19 prevention. This model can apply to other regions because the proportion of acquaintances and strangers could auto-adjust in the fitting process. It is also suitable for other infectious diseases.

Ethics statement

This study does not involve human participants and animal subjects.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare no competing interests.

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Contributors

DL and QT are joint first authors, contributed equally to this article for drafting the manuscript. BS and LZ conceived and designed the study. QT, MP and YW collected the epidemiological data of each province in Mainland China. BS and DL analyzed the date with the help of YW and MP. DL and QT drafted the manuscript. BS and LZ revised the manuscript critically. All authors reviewed and approved the final manuscript. LZ (ZHANGLEI_FKYY@163.COM) and BS (subo_group@hotmail.com) are the co-corresponding authors and the guarantors. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Tables

Table 1. The definition and setting range of parameters in ScEIQR model

Parameters	Definition	Method	Setting range
Sc	contactable susceptible under the social NPIs	MCMC	[1, 0.01N]
β'	transmission rate, the number of infected people by one infector	MCMC	[1,19]
σ	transition rate from exposure to being contagious	MCMC	[0.27,0.5]
γ	recovery rate of asymptomatic infector	MCMC	[0.04,0.3]
η	hospitalization rate and pace of symptomatic infectors	MCMC	[0.001,0.999]
κ	extent of epidemiological investigations	MCMC	[0,350]
ρ	positive rate of COVID-19 in quarantined people	MCMC	[0,0.1]
ω	transited rate of quarantined people developing to contagious per day	MCMC	[0.07,0.6]
CR	the proportion of contactable susceptible (Sc) under the interventive social prevention	Sc/N	-
Ipd	the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent	1/σ+1/η	-
utI%	the proportion of untraceable infectors, approximately equates to the asymptomatic	γ/(η+κρη+γ).	-
SurveyQ	the quality of contact tracing	κ•ρ	-
Cpd	the time for untraceable infectors with contagious among susceptible	1/γ	-

Abbreviation: Ipd: Incubation period; Cpd: communicable period; utI%: Proportion of asymptomatic infectors; N: the total population of a province. * Details in the supplementary methods

Table 2. The median value of parameters and indexes in 29 provinces of mainland China usingthe ScEIQR model.

Variables	Median	IQR 25%, 75%	Range
β'	10.22	8.47, 12.35	3.29-15.06
σ	0.42	0.40, 0.44	0.33-0.48
γ	0.15	0.10, 0.22	0.05-0.26
η	0.69	0.47, 0.87	0.16-0.97
κ	42.0	27.83, 60.78	5.35-147.79
ρ (%)	0.9%	0.4%-1.6%	0.03%-5.10%
ω	0.12	0.10, 0.15	0.07-0.21
Sc	26.98	13.97, 54.57	5.91-25525.54
CR	6.84E-07	3.77E-07, 1.44E-06	1.64E-07-4.33E-04
Ipd	4.17	3.60, 4.71	3.27-9.62
utI%	14.88%	8.17%, 25.37%	3.92%-34.36%

SurveyQ	0.39	0.22, 0.55	0.04-2.61
Cpd	6.77	4.53, 10.36	3.91-19.90
1/σ	2.39	2.26, 2.56	2.07-3.01

Abbreviation: Ipd: Incubation period; utI%: Proportion of asymptomatic infectors; Cpd: communicable period

Figure legend

Figure 1. The flow diagram of ScEIQR epidemiological model

Six compartments: contactable susceptible (Sc), exposed individuals (E), infected individuals who were outsides of the public health measures (I), close contacts being in quarantine (Q), self-recovery individuals (Rs) and the cumulative hospitalized individuals (Rh). The flow velocities between the compartments are indicated.

Figure 2. The fitting curves of confirmed cases and close contacts predicted by the ScEIQR model from Day 0, -Jan. 23, 2020

A: The fitting curves of confirmed cases and close contacts in Beijing, representing North China.

B: The fitting curves of confirmed cases and close contacts in Liaoning, representing Northeast China.

C: The fitting curves of confirmed cases and close contacts in Jiangxi, representing East China.

D: The fitting curves of confirmed cases and close contacts in Guangdong, representing South China.

E: The fitting curves of confirmed cases and close contacts in Gansu, representing Northwest China.

F: The fitting curves of confirmed cases and close contacts in Sichuan, representing Southwest China.

G: The fitting curves of confirmed cases and close contacts in Hubei, representing Central China.

Figure 3. The association between air temperature and transmission rates (β') of COVID-19

A, B: A, the transmission rates of COVID-19 among acquaintances for the 29 provinces grouped by geographical regions. B Mapping the transmission rate of COVID-19 in 29 provinces of mainland China. In Figures A and B, the number represents the provinces of each geographical region. North China: 1-5; Northeast China: 6-8; East China: 9-15; Central China: 16-18; South China: 19-21; Northwest China: 22-25; Southwest: 26-29.

C. Mapping the daily mean temperature from Jan. 15, 2020 to the Feb. 15.2020 in 29 provinces of mainland China.

D: The association between daily minimum temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

E: The association between daily mean temperature and the transmission rate, β' of COVID-19 depicted by LOESS.

F: The association between daily maximum temperature and the transmission rate, β' of COVID-19 depicted LOESS. The dots with different color represent the temperature in different provinces.

Figure 4. Evaluation of the three NPI measures' effectiveness and the suppositional simulation

A: The model was used to calculate CR for 28 provinces. In B, C, E, F, H, and I Figures, the solid curves are the fitted curves in our modeling analysis. The dashed lines represent the suppositional simulation curves after adjusting three NPI measures' value. The small dashed line shows the up-regulation of the NPI measures' values, and the big dashed line shows the down-regulation of the NPI measures' value. The red curves represent Rh 's compartment; the purple curve represents the Q compartment; the orange curve represents the I compartment.

B: The change in Rh, Q, and I compartment after adjusting the CR 30%-up or down.

C: The change in Rh, Q, and I compartment after adjusting the CR 50%-up/down.

D: The hospitalization rate and pace, η, in the 29 provinces.

E: The change in Rh, Q, and I compartment after adjusting η 30% -up/down.

F: The change in Rh, Q, and I compartment after adjusting η 50% -up/down.

G: The quality of contact tracing, surveyQ was depicted among 29 provinces.

H: The simulation of Rh, Q, and I compartment after adjustment of κ for 1/3 down or three times up.

I: The simulation of Rh, Q, and I compartments after adjustment of ρ- 1/3 down or three times up.

Figure 5. The transmission patterns of COVID-19 under social NPIs and the association of untraceable infectors with surveyQ, η, and air temperature.

A: A representative example of intra-family and inter-family transmission of COVID-19 in Beijing.

B: A representative example of COVID-19 transmission among strangers in a large mall.

C: Stranger-stranger transmission is the blind zone of contact tracing.

D: The median proportion of asymptomatic infectors among 29 provinces.

E: The nonlinear association between the ratio of untraceable infectors and surveyQ. Higher surveyQ could reduce the ratio of untraceable infectors. However, as the surveyQ increases, the proportion of untraceable infectors remains constant.

F: The nonlinear association between the ratio of untraceable infectors and η. Higher η could reduce the ratio of untraceable infectors either.

G: The relationship between the ratio of untraceable infectors and the daily mean temperature.

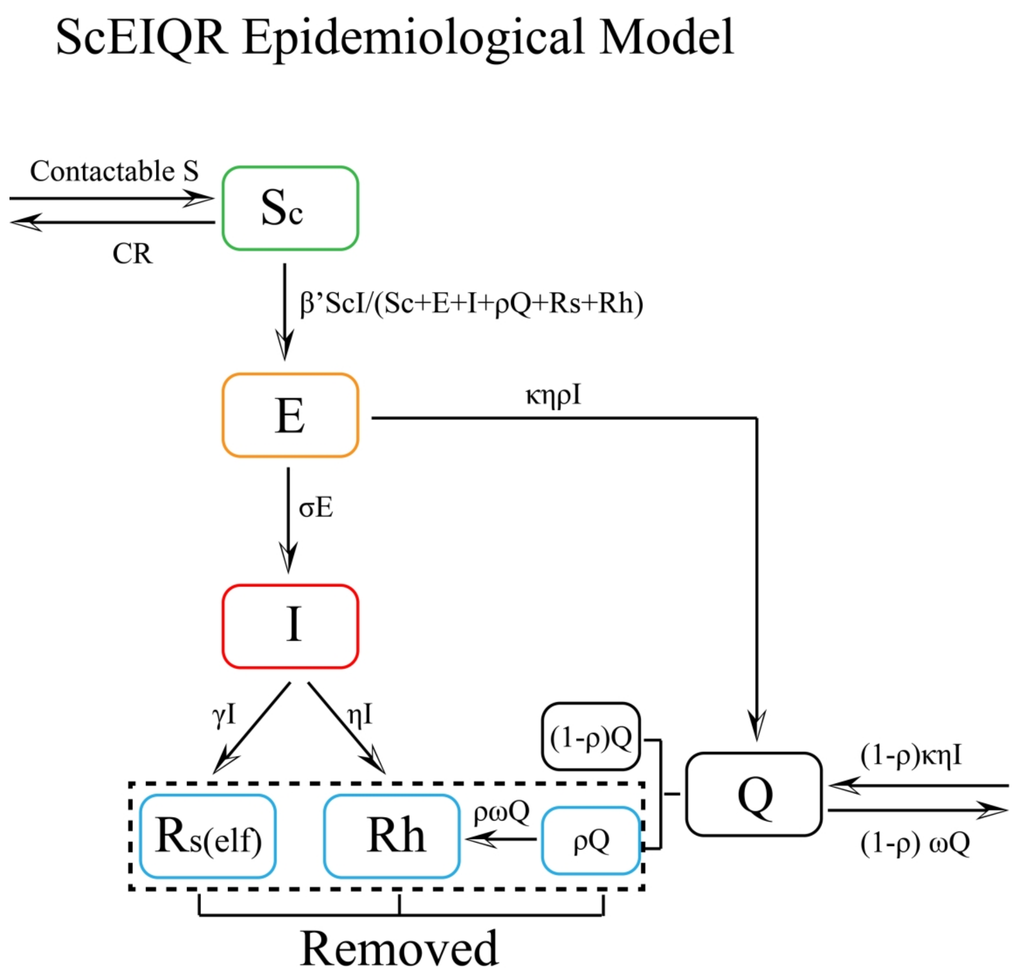

Figure 1

Figure 1

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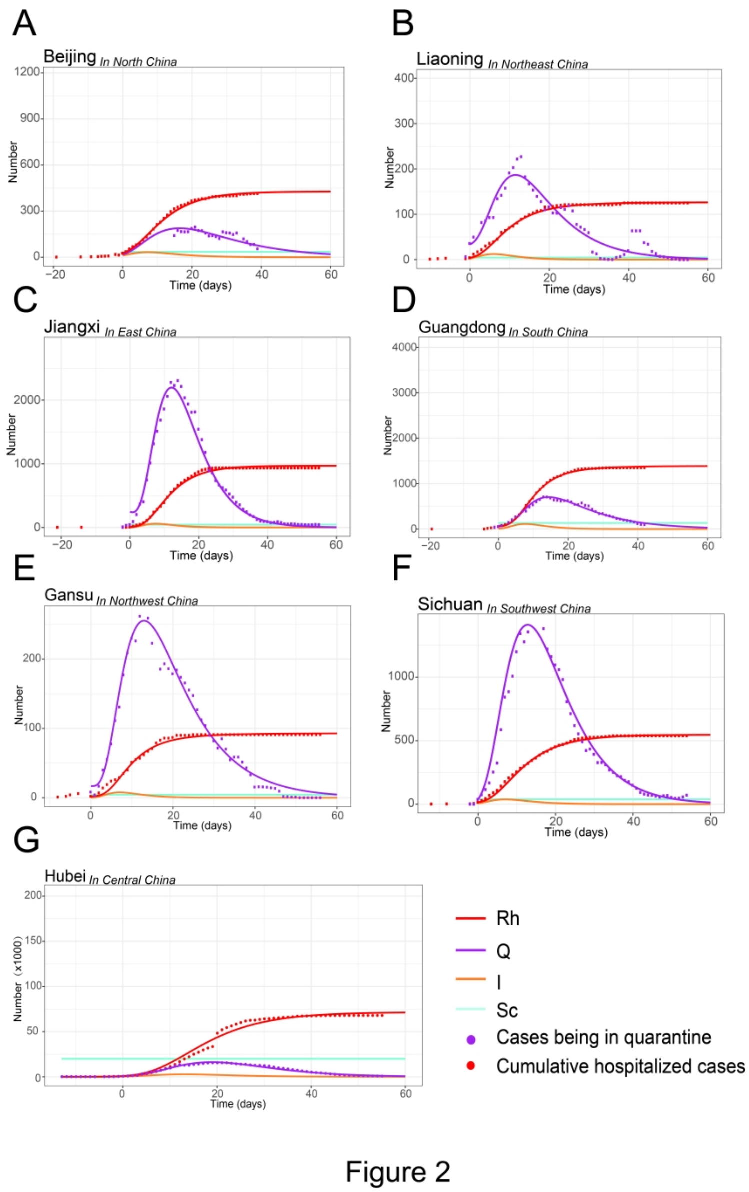

Figure 2

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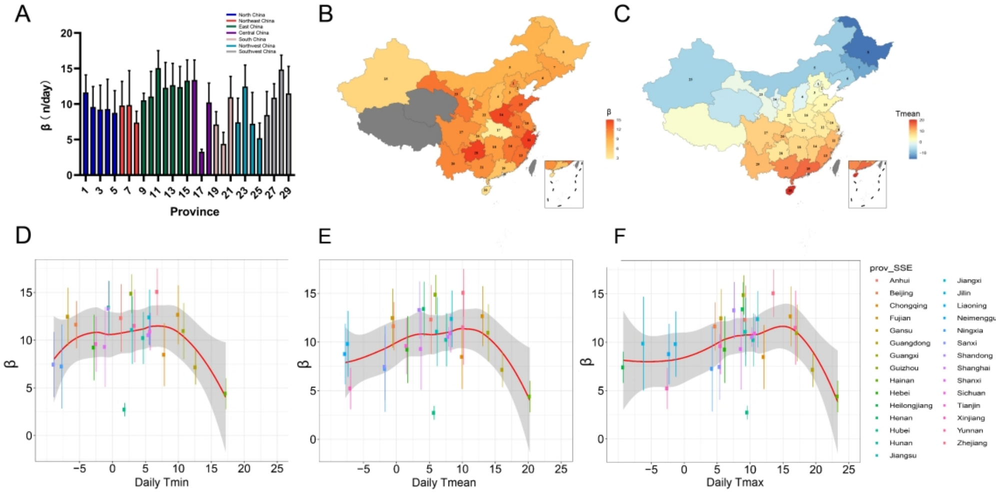

Figure 3

Figure 3

356x203mm (300 x 300 DPI)

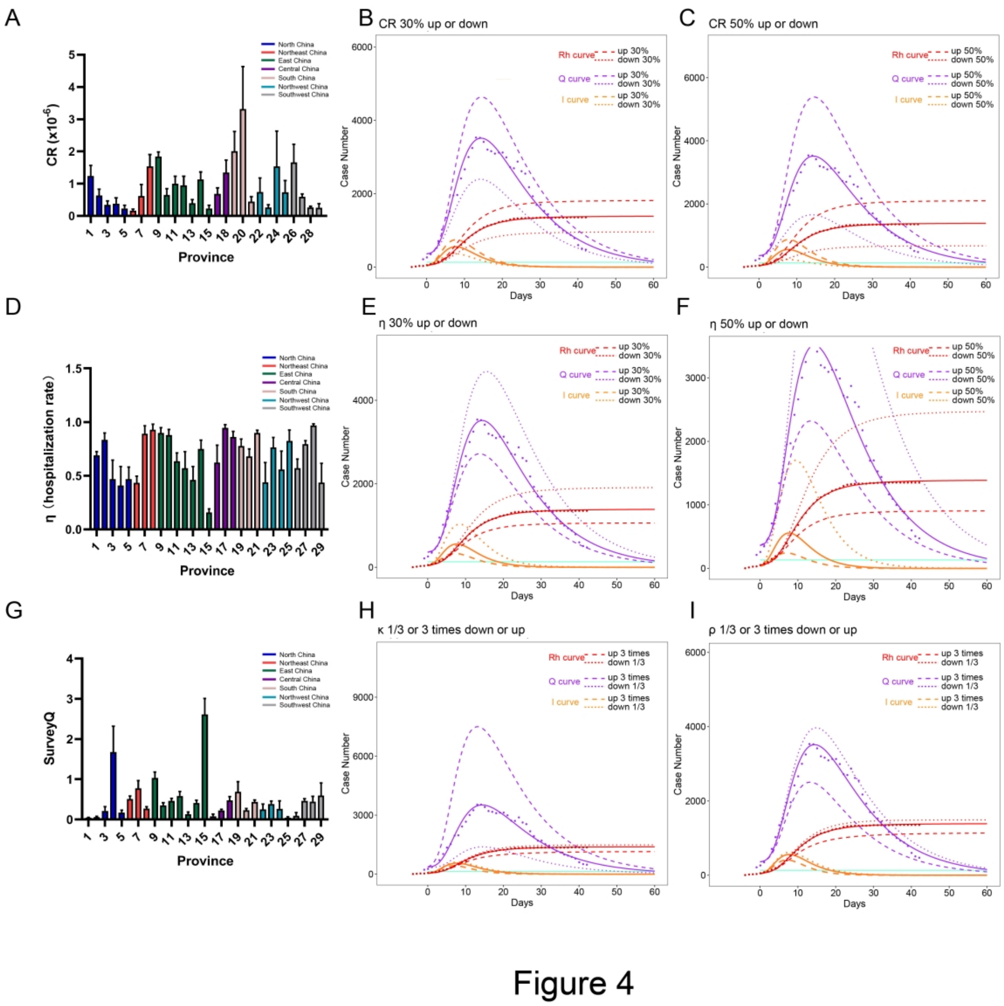

Figure 4

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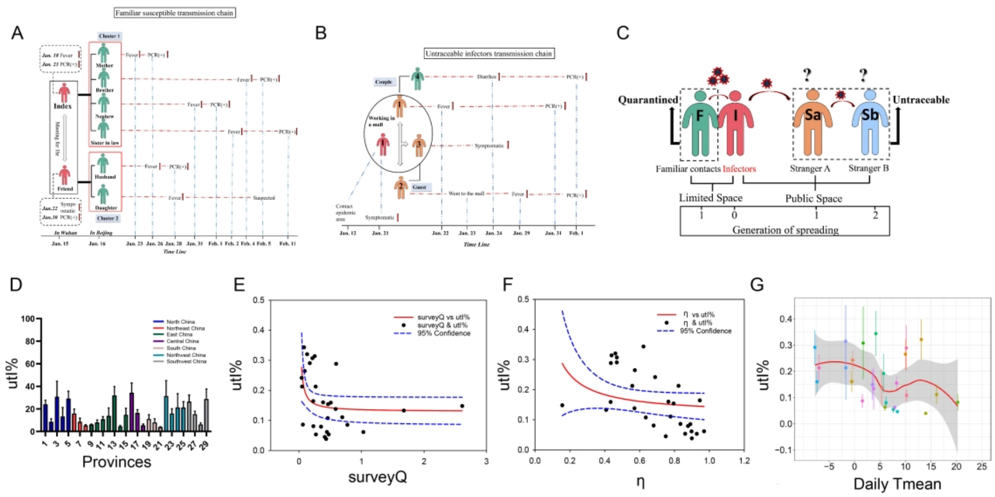

Figure 5

Figure 5

401x218mm (300 x 300 DPI)

The impact of air temperature and containment measures on mitigating the intra-household transmission of SARS-CoV-2 : a data-based modeling analysis

Di Liu [*,1], Qidong Tai [*,2], Yaping Wang [3], Miao Pu [3], Lei Zhang [†,2], Bo Su [†,1]

Supplementary methods

The stochastic ScEIQR epidemiological model

To simulate the epidemiological data of COVID-19 intra-household transmission under NPIs implementation, we developed an early spreading, early non-pharmaceutical-intervention stochastic model, denoted as ScEIQR model. The flow diagram of ScEIQR model was as the following, which demonstrated as following:

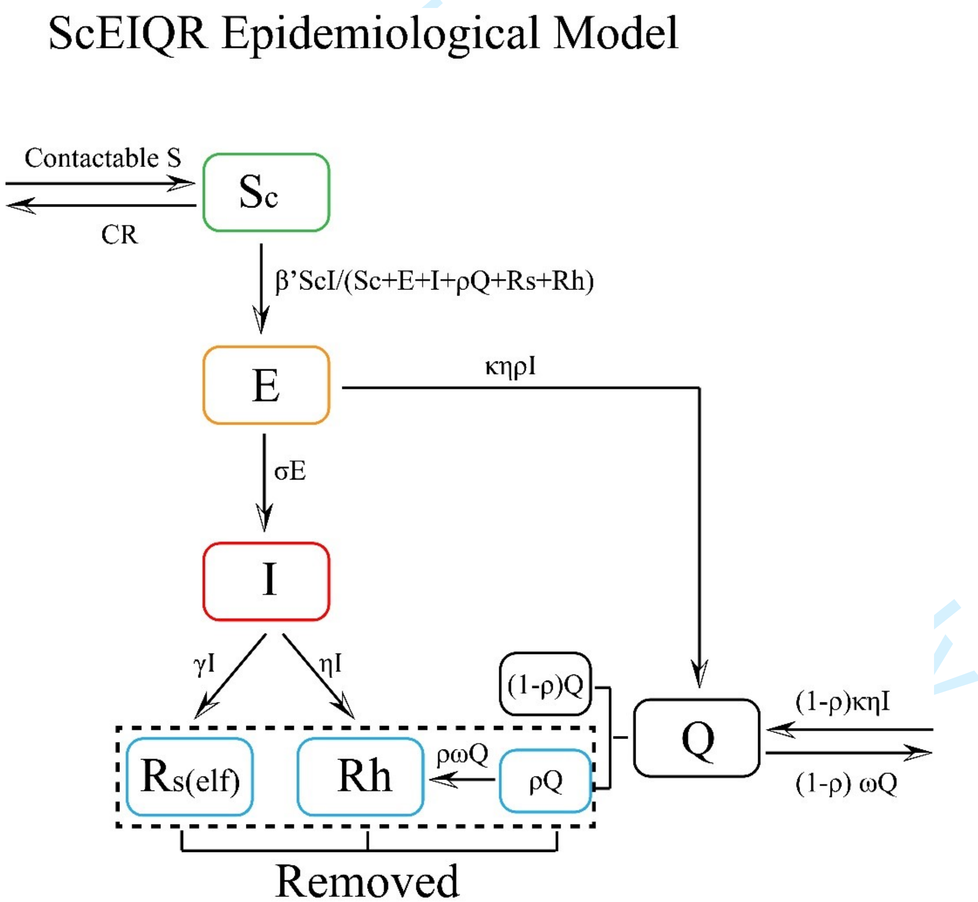

Figure 1

Compartments of the stochastic ScEIQR model

Sc: The contactable susceptible subpopulation for the infectors, comprised of their family, relatives, co-workers, friends, and some strangers who could be contacted by the infector under the interventive social prevention. The initial Sc is defined as a continuous random variable with Gaussian distribution in the model. The left arrow of Sc means the susceptible could be entered into this compartment to become the contactable susceptible (just a part of the susceptible) at the rate of c.

E: The exposed individuals who are in the incubation period after effective contact with the infectors.

I: The infectors, either immigrant or local reproductive infectors who are still outsides of the public health measures.

Q: The close contacts of infectors found out by epidemiological survey, and notified to be in self-quarantine at home, in the hotel or indicated isolating room for 14-day medical observation. The Q value in this model is the daily reported cumulative close contacts or entry of medical observation minus the daily cumulative dismission of medical observation for each province. The right arrow of Q means the quarantined individuals who are not be diagnosed as infectious leave the compartment Q to be the susceptible again at the rate of $(1\text{-}\rho)\ \omega Q$, the opposite arrow means the susceptible in close contacts (in fact, only a small part of close contacts in contact tracing were infected, and the other were still the susceptible) enter the compartment Q at the rate of $(1\text{-}\rho)\kappa\eta I$.

Rs(elf): No all the infectious may see a doctor, especially the non-symptoms infectors. Some of the COVID-19 cases can be self-healing. Thus, the self-recovery individuals who have never be diagnosed and hospitalized because of mild symptoms, or asymptomatic infection, and thus were not be recorded in the daily official epidemic reports is designated as Rs.

Rh: The cumulative individuals who were etiologically diagnosed (mostly SARS-CoV-2 RNA rtPCR positive in oropharyngeal swabs, and inconsistent with other clinical symptoms) and hospitalized in isolate wards. The cumulative number includes any hospitalizing, or dead, or cured COVID-19 patients. In China, every confirmed case had been hospitalized in isolation wards, he/she cannot infect others, so can be regarded as removed.

Removed: The removed means any infectors who have been deprived of the ability to propagate, either by the gain of immunity (Rs, cured in Rh) or by public health measures (infectors in Q, the hospitalizing in Rh), or death (the dead in Rh). The removed in this model is the sum of cumulative Rs, Rh, and the positive cases in Q. So, the flow velocity to Rs and Rh was different.

Model validation

The value of parameters was randomly sampled with one of MCMC method, Metropolis-Hastings (M-H) algorithm, and documented under an appropriate tolerance of best fitting with at least 100000 iterations of 0.1 step size from 0 to 60 days with burn-in of 50000 iterations for every province of Mainland China.

Other indexes

CR: restriction factor, the proportion of contactable susceptible (Sc) over the total population of a province under the interventive social prevention, which is simply calculated as Sc/N.

utI%: the proportion of the self-recovery removed, including asymptomatic infections or any infection without hospitalization and report, which were estimated as $\gamma/(\eta+\kappa\rho\eta+\gamma)$.

SurveyQ: an estimation for the quality of the epidemical survey, which is calculated as $\kappa\bullet\rho$.

Incubation period: The incubation period was the time elapsed from exposure to SARS-COV-2 to the symptoms firstly apparent, calculated with $1/\sigma+1/\eta$.

Communicable period: The time for untraceable infectors with contagious among susceptible, calculating with $1/\gamma$.

The air temperature of every province during the COVID-19 outbreak and spreading

The historical meteorological data were collected from china's meteorological administration. The daily mean air temperature was calculated from Jan 15, 2020 to Feb 15, 2020, i.e., from a week before Jan 23, 2020, to 3 weeks after that. In this period, COVID-19 began spreading and controlled by NPI in most of the provinces of China, except Hubei.

The epidemical data and epidemical survey of 31 provinces

The daily confirmed and quarantined cases were used for fitting the model. Almost all the diagnosed cases were hospitalized in isolation wards simultaneously according to the Guidance, thus the reported confirmed cases were just the hospitalized infectors in China. Cases confirmed with a laboratory test of the same sample identified two targets positive detection with real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assay or high-throughput sequencing, one is ORF, another one is the N protein of SARS-CoV-2. The quarantined cases were the population close contact the confirmed cases, asymptomatic infections, and suspected cases identified with epidemiological investigation within 24 hours. The close contacts were including:

1) living, studying, working in the same house with the confirmed or suspected cases.

2) medical staff, family members, or other persons who have close contact with cases in the process of diagnosis, treatment, or nursing.

3) take the same transport and have close contact with infectors, including caregivers, peers, or other passengers(*31*).

The quarantined people were isolated in the home or a specific place for observation of their symptoms for 14 days. If the lab testing results of close contacts of confirmed cases and asymptomatic infections are negative during the medical observation period, they still need to continue quarantine until the end of the observation of 14 days. Those who are in close contact with suspected cases can be relieved of medical observation when suspected cases are excluded from infection.

The provinces of China

There are 34 provincial-level administrative divisions of China, including 23 provinces, 4 municipalities (Beijing, Tianjin, Shanghai, Chongqing), 5 autonomous regions (Guangxi, Inner Mongolia, Tibet, Ningxia, Xinjiang) and 2 special administrative regions (Hong Kong, Macau). 23 provinces are including Anhui, Fujian, Gansu, Guangdong, Guizhou, Hainan, Hebei, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Liaoning, Qinghai, Shaanxi, Shandong, Shanxi, Sichuan, Yunnan, Zhejiang, Taiwan. Seven geographical regions were classified as Mainland China, named as North China, Northeast China, East China, Central China, South China, Northwest China, Southwest China. The 29 provinces were included in our study, and they were separated into each geographical region and represented by numbers as follows:

1) North China: Beijing, Tianjin, Hebei, Shanxi, Inner Mongolia (1-5);

2) Northeast China: Liaoning, Jilin, Heilongjiang (6-8);

3) East China: Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong (9-15) and Taiwan;

4) Central China: Henan, Hubei, and Hunan (16-18);

5) South China: Guangdong, Hainan, Guangxi (19-21), Hongkong, and Macau;

6) Northwest China: Shaanxi, Gansu, Ningxia, Xinjiang (22-25) and Qinghai;

7) Southwest China: Chongqing, Sichuan, Guizhou, Yunnan (26-29), and Tibet.

Supplementary tables

Table S1. The mean value of parameters and indexes in each province of mainland China

	Parameters and indexes (Mean±SD)										
Province	**β’**	**σ**	**γ**	**η**	**κ**	**ρ(%)**	**ω**	**CR**	**Ipd (day)**	**utI%**	**Survey Q**
All provinces	10.01±2.86	0.42±0.04	0.16±0.07	0.68±0.20	45.55±28.66	1.32±1.30	0.12±0.03	1.58E-05±7.88E-05	4.31±1.18	15.63±9.27	0.46±0.53
Beijing	11.63±2.48	0.35±0.02	0.23±0.05	0.69±0.04	5.59±0.17	0.78±0.12	0.07±0	1.24E-06±3.24E-07	4.34±0.19	24.22±3.57	0.04±0.01
Tianjin	9.58±2.89	0.33±0.03	0.08±0.03	0.83±0.06	12.79±0.72	0.49±0.12	0.07±0	6.35E-07±1.95E-07	3.71±0.3	8.7±2.58	0.06±0.02
Hebei	9.22±3.44	0.41±0.06	0.22±0.06	0.47±0.18	46.56±6.34	0.47±0.24	0.16±0.02	3.38E-07±1.27E-07	5.05±1.07	30.75±13.89	0.22±0.11
Shanxi	9.29±4.2	0.41±0.05	0.14±0.07	0.41±0.18	65.78±15.26	2.49±0.57	0.14±0.02	3.77E-07±1.82E-07	3.89±1.29	13.35±7.9	1.68±0.64
Neimenggu	8.77±3.12	0.44±0.03	0.22±0.04	0.47±0.11	62.99±5.38	0.27±0.08	0.15±0.01	2.34E-07±9.11E-08	4.55±0.59	29.11±6.61	0.17±0.06
Liaoning	9.81±3.38	0.48±0.02	0.13±0.04	0.43±0.06	27.96±1.68	1.82±0.27	0.12±0.01	1.64E-07±5.09E-08	4.46±0.35	15.98±4.01	0.51±0.08
Jilin	9.85±4.85	0.41±0.06	0.15±0.06	0.89±0.07	58.58±14.51	1.35±0.28	0.13±0.03	6.15E-07±3.60E-07	3.6±0.38	8.62±3.27	0.77±0.2
Heilongjiang	7.39±1.62	0.44±0.03	0.07±0.01	0.93±0.05	27.83±1.98	0.98±0.16	0.11±0.01	1.53E-06±3.76E-07	3.35±0.19	5.43±0.73	0.27±0.05

Shanghai	10.53±1.01	0.41±0.07	0.12±0.01	0.9±0.05	64.41±2.25	1.6±0.19	0.21±0.02	1.84E-06±1.44E-07	5.44±0.54	6.22±0.42	1.03±0.15
Jiangsu	11.06±3.55	0.44±0.04	0.1±0.03	0.88±0.05	32.43±3.1	1.08±0.12	0.15±0.01	6.53E-07±1.96E-07	3.45±0.24	8.01±2.27	0.35±0.06
Zhejiang	15.06±2.46	0.48±0.02	0.11±0.03	0.64±0.08	34.64±2.55	1.33±0.16	0.1±0.01	1.00E-06±2.37E-07	3.67±0.24	10.83±2.35	0.46±0.06
Anhui	12.31±3.55	0.38±0.03	0.14±0.07	0.57±0.15	36.65±4.4	1.61±0.29	0.13±0.01	9.51E-07±2.86E-07	4.55±0.55	13.88±7.03	0.59±0.11
Fujian	12.66±3.09	0.45±0.03	0.23±0.04	0.46±0.12	42.01±2.93	0.31±0.14	0.13±0.01	3.89E-07±1.17E-07	4.55±0.61	32.08±7.71	0.13±0.06
Jiangxi	12.38±2.91	0.41±0.03	0.05±0.01	0.75±0.08	48.15±2.52	0.86±0.11	0.16±0.01	1.13E-06±2.36E-07	3.81±0.18	4.59±0.8	0.41±0.07
Shandong	13.3±2.94	0.35±0.06	0.1±0.06	0.16±0.03	51.26±3.2	5.09±0.69	0.08±0.01	2.36E-07±9.04E-08	9.62±1.3	14.88±5.82	2.61±0.4
Henan	13.4±2.8	0.45±0.03	0.26±0.03	0.62±0.16	24.87±2.71	0.31±0.18	0.12±0.01	6.84E-07±1.90E-07	4.56±0.95	34.36±8.6	0.08±0.05
Hubei	3.29±0.34	0.42±0.05	0.23±0.04	0.95±0.03	5.35±0.62	4.28±0.48	0.11±0.01	4.33E-04±8.35E-05	3.48±0.29	16.49±2.9	0.23±0.03
Hunan	10.22±2.73	0.45±0.03	0.07±0.01	0.86±0.05	38.98±2.47	1.22±0.2	0.16±0.01	1.35E-06±3.82E-07	3.42±0.19	5.44±1.2	0.48±0.09
Guangdong	7.14±1.79	0.44±0.04	0.16±0.06	0.78±0.06	14.33±1.33	4.87±1.82	0.17±0.02	2.01E-06±6.07E-07	3.58±0.26	11.14±3.78	0.69±0.25
Hainan	4.39±1.63	0.44±0.04	0.07±0.03	0.68±0.07	23.03±1.83	1±0.18	0.08±0.01	3.32E-06±1.31E-06	3.78±0.25	8.17±3.17	0.23±0.05
Guangxi	10.95±2.94	0.46±0.02	0.05±0	0.9±0.03	52.88±2.53	0.82±0.08	0.11±0	4.45E-07±1.51E-07	3.27±0.13	3.92±0.3	0.43±0.05
Shaanxi	7.44±3.41	0.4±0.05	0.22±0.05	0.44±0.18	76.13±8.4	0.33±0.17	0.1±0.01	7.43E-07±4.38E-07	5.52±1.91	31.44±13.72	0.25±0.13
Gansu	12.46±3.04	0.45±0.03	0.2±0.05	0.76±0.09	41.99±3.6	0.92±0.14	0.1±0.01	2.66E-07±7.72E-08	3.56±0.27	16.08±4.02	0.39±0.07
Ningxia	7.24±4.41	0.36±0.06	0.17±0.07	0.56±0.17	70.9±11.44	0.37±0.26	0.11±0.02	1.53E-06±1.10E-06	4.91±1.29	21.31±12.15	0.27±0.19
Xinjiang	5.21±2.13	0.41±0.05	0.23±0.05	0.82±0.1	147.79±11.06	0.03±0.01	0.08±0	7.34E-07±3.67E-07	3.71±0.32	21.32±5.08	0.05±0.02
Chongqing	8.47±3.31	0.42±0.03	0.22±0.04	0.57±0.08	39.36±6.01	0.22±0.16	0.13±0.01	1.66E-06±5.67E-07	4.17±0.34	26.52±5.82	0.09±0.08
Sichuan	10.9±1.96	0.38±0.03	0.21±0.04	0.79±0.03	46.84±3.25	0.99±0.07	0.12±0.01	5.92E-07±9.07E-08	3.89±0.22	15.47±2.48	0.47±0.05
Guizhou	14.87±2.03	0.35±0.03	0.09±0.02	0.97±0.02	23.7±3.5	1.86±0.37	0.17±0.02	2.63E-07±3.44E-08	3.92±0.25	6.25±1.45	0.45±0.13
Yunnan	11.49±3.82	0.44±0.04	0.25±0.04	0.44±0.18	97.33±33.65	0.59±0.19	0.15±0.04	2.60E-07±1.18E-07	5.14±1.62	28.89±8.82	0.59±0.31

Abbreviation: Ipd: Incubation period; utI%: Proportion of Untraceable infectors;

Supplementary figure legend

Figure S1. The fitting curves of both the number of daily cumulative confirmed cases and close contacts being in quarantine in 22 provinces of Mainland China (Day 0, the 23rd, Jan, 2020).

A: The fitting curve of provinces in Northwest China- Xinjiang/ Shaanxi/ Ningxia and Central China-Hunan/ Henan.

B: The fitting curve of provinces in South China- Hainan/ Guangxi, and Southwest China-Yunnan/ Guizhou/ Chongqing.

C: The fitting curve of provinces in East China- Shanghai/ Zhejiang/ Anhui/ Fujian/ Shandong/ Jiangsu.

D: The fitting curve of provinces in North China- Neimenggu/ Tianjin/ Hebei/ Shanxi and Northeast China-Heilongjiang/ Jilin.

Figure S2. Suppositional simulation of contact tracing parameters, κ and ρ.

A-B: The median κ and ρ was calculated among 29 provinces.

C-D: The influence on Rh, Q and I compartment after adjustment of κ by 30% or 50%.

E-F: The simulated Rh, Q and I compartment after adjustment of ρ by 30% or 50%.

Figure S3. The median incubation period of COVID-19 among 29 provinces.

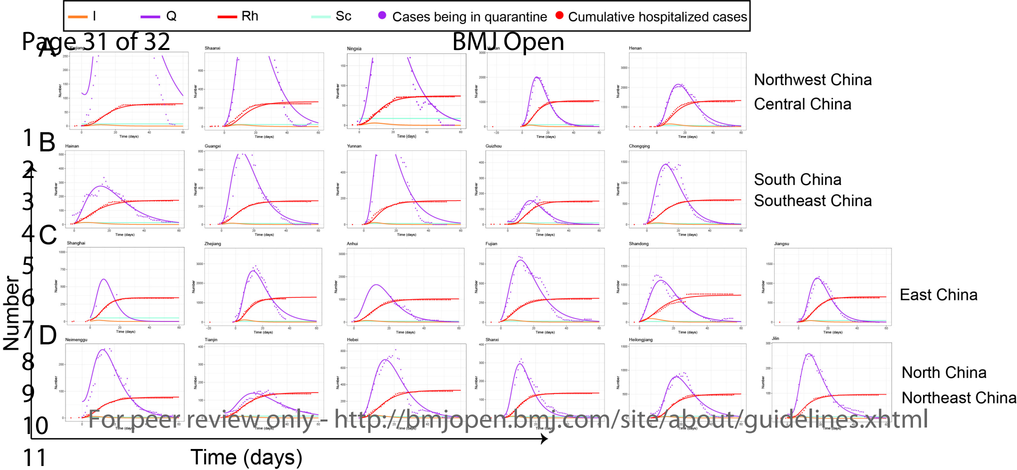
I
Q
Rh
Sc
Cases being in quarantine
Cumulative hospitalized cases
A
Xinjiang
Shaanxi
Ningxia
Hubei
Henan
Northwest China
Central China
B
Hainan
Guangxi
Yunnan
Guizhou
Chongqing
South China
Southeast China
C
Shanghai
Zhejiang
Anhui
Fujian
Shandong
Jiangsu
East China
D
Neimenggu
Tianjin
Hebei
Shanxi
Heilongjiang
Jilin
North China
Northeast China
Number
Time (days)

Figure S1

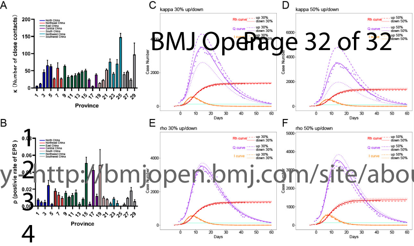
A
κ (Number of close contacts)
North China
Northeast China
East China
Central China
South China
Northwest China
Southwest China
Province
B
ρ (postivie rate of EPS)
Province
C
kappa 30% up/down
Rh curve
Q curve
I curve
up 30%
down 30%
Case Number
Days
D
kappa 50% up/down
up 50%
down 50%
E
rho 30% up/down
F
rho 50% up/down

Figure S2

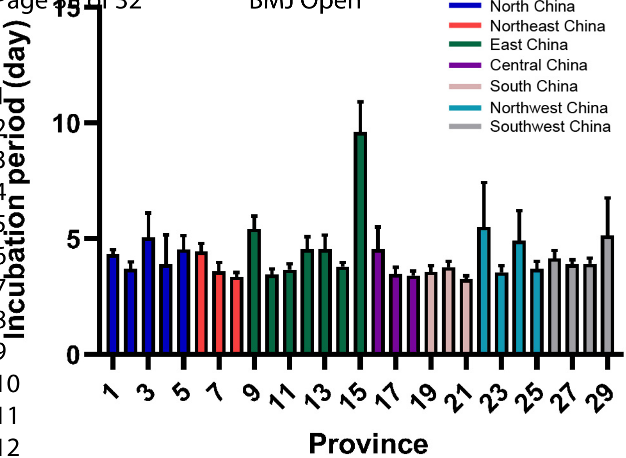
Incubation period (day)
15
10
5
0
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
Province
North China
Northeast China
East China
Central China
South China
Northwest China
Southwest China

Figure S3