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Notifiable Infectious Diseases Reports

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Cover photo: China CDC Professionals of the Confirming Novel Coronavirus Team Analyse the Testing Results. (Photographer: Lanyu Li from National Institute for Viral Diseases Control and Prevention, China CDC)

Notes from the Field

Description of the First Strain of 2019-nCoV, C-Tan-nCoV Wuhan Strain — National Pathogen Resource Center, China, 2020

Qiang Wei[1,&]; Yanhai Wang[2,&]; Juncai Ma[3,&]; Jun Han[2]; Mengnan Jiang[1]; Li Zhao[2]; Fei Ye[2]; Jingdong Song[2]; Bo Liu[1]; Linhuan Wu[3]; Wenjie Tan[2,#]; Guizhen Wu[2,#]; George F. Gao[1]; Jianjun Liu[1,#]

The recent outbreak of novel coronavirus-infected pneumonia (NCIP) in China (*1*) has attracted much attention domestically and internationally. As the outbreak occurred, China carried out emergency responses quickly, notified the World Health Organization (WHO) in a timely manner, and shared the viral gene sequence with international communities immediately after pathogenic identification.

The timely release of information on the novel coronavirus (2019-nCoV), joint research on relevant viral genome mutations, pathogenicity, and transmission mechanisms, vaccine development, and drug screening and evaluation are of great significance for epidemic prevention and control. Therefore, for prevention and control of the NCIP epidemic and for future scientific research on 2019-nCoV, the National Pathogen Resource Center (NPRC) published information of the first strain of 2019-nCoV on the National Science and Technology Resource System for Novel Coronavirus (http://nmdc.cn/#/nCoV) on January 24, 2020.

Virus Isolation

Researchers from the National Institute for Viral Disease Control and Prevention (IVDC) of China CDC successfully isolated the virus out of lower respiratory alveolar lavage fluid from patients with unexplained viral pneumonia in Wuhan and detected typical electron microscopic coronavirus morphology on January 6, 2020, which substantiated the successful isolation and culture of the first 2019-nCoV strain in China (*2*).

Strain Basic Information

Basic strain information of 2019-nCoV is important basis for downstream sharing, use, research, and epidemic prevention and control. With in-depth study of its biological traits and pathogenicity, further information will be supplemented gradually. (Table 1)

TABLE 1. Basic information for the first strain of 2019-nCoV.

Descriptors	Description
Code	CHPC 2020.00001, NPRC 2020.00001
Name in Chinese	新型冠状病毒武汉株01
Name in English	C-Tan-nCoV Wuhan Strain
Taxonomy	Novel β genus coronavirus
Source of the Specimen	Clinical Patients
Source of Collection	Wuhan, Hubei Province, China
Isolation Date	Jan 6, 2020
Risk Level	BSL-3
Contact Info	ivdcolm@ivdc.chinacdc.cn, chpc@chinacdc.cn

Note: CHPC refers to the Center for Human Pathogen Collection of China CDC, and NPRC refers to the National Pathogen Resource Center of China.

Specific Primers and Probes for Detecting 2019-nCoV (*3*)(Table 2)

TABLE 2. Real-time RT-PCR. The open reading frame 1ab (ORF1ab) and the nucleoprotein N gene region of the virus were recommended for primers and probes.

Item	Sequence
Target 1 (ORF1ab)	
Forward primer (F)	CCCTGTGGGTTTTACACTTAA
Reverse primer (R)	ACGATTGTGCATCAGCTGA
Fluorescent probes (P)	5’-FAM-CCGTCTGCGGTATGTGGAA AGGTTATGG-BHQ1-3’
Target 2 (N)	
Forward primer (F)	GGGGAACTTCTCCTGCTAGAAT
Reverse primer (R)	CAGACATTTTGCTCTCAAGCTG
Fluorescent probes (P)	5’-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3’

Note: Results reading: negative (no Ct value or Ct=40); positive (Ct value <37, considered positive); and suspicious (if Ct value is between 37 and 40, repeat testing is recommended). If Ct value <40 in repeat testing and distinctive peaks are observed in the amplification curve, the sample is considered positive; otherwise, the sample is considered negative.

Strain Imaging

Negatively stained 2019-nCoV particles generally present a spherical shape with some pleomorphism. The viral particles range from 60–140 nm in diameter. Discernable spikes of 9–12 nm on the envelope render the virions appearance of a solar corona (hence named coronavirus) (Figure 1).

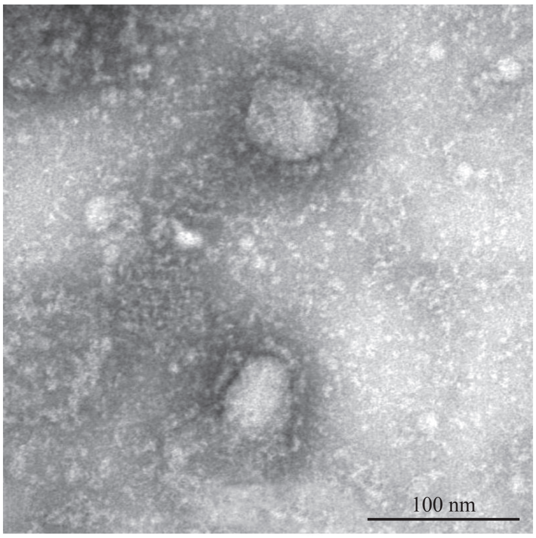

FIGURE 1. Negatively stained 2019-nCoV particles in the supernatant of infected cells culture.

Strain Sharing

The 2019-nCoV strains can be shared for external use under proper administrative approvals and specified conditions. Users must indicate the source of the strains on relevant materials, including but not limited to publications and awards, as the following: National Pathogen Resource Center (National Institute for Viral Disease Control and Prevention, China CDC) with the NPRC number. Upon completion of the specified activities, users should return the strains to NPRC (IVDC) or perform proper destruction and disposal and issue a description of use to NPRC.

NPRC is a national science and technology resource sharing service platform established by China CDC. As a National Scientific and Technological Innovation Center, it is mainly responsible for the collection, identification, labeling, preservation, and provision of national pathogenic microbial resources. Through systemic integration of pathogenic microbial resources and enhancement of utility efficiency, NPRC is contributing to scientific and technological development as well as social welfare with its lasting conviction for a sharing and open society.

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References

1. Tan WJ, Zhao X, Ma XJ, Wang WL, Niu PH, Xu WB, et al. A novel coronavirus genome identified in a cluster of pneumonia cases — Wuhan, China 2019–2020. China CDC Weekly 2020;2(4):61–2. http://weekly.chinacdc.cn/en/article/ccdcw/2020/4/61.
2. Zhu N, Zhang DY, Wang WL, Li LW, Yang B, Song JD, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. [2020-1-24]. http://dx.doi.org/10.1056/NEJMoa2001017.
3. Institute of Virus Disease Control and Prevention, China CDC. Primers and probes for detection of the novel coronavirus. [2020-1-21]. http://ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.html. (In Chinese).

Notes from the Field

Epidemic Update and Risk Assessment of 2019 Novel Coronavirus — China, January 28, 2020

Wenxiao Tu[1]; Houlin Tang[2]; Fangfang Chen[2]; Yinong Wei[1]; Tingling Xu[3]; Kaiju Liao[4]; Nijian Xiang[1]; Guoqing Shi[1]; Qun Li[1]; Zijian Feng[1,#]

Background

On December 29, 2019, the health authorities in Hubei Province and Wuhan City received a report of a cluster of pneumonia cases of unknown etiology from a local hospital, and all four patients were employees of the Wuhan Huanan Seafood Wholesale Market (HN market for short) (*1*). By January 8, 2020, Chinese authorities had identified a new virus 2019 novel coronavirus (2019-nCoV) linked with the outbreak of disease, which has been named novel coronavirus-infected pneumonia (NCIP) (*2*). On 15 January, the National Health Commission (NHC) issued guidelines for the diagnosis, treatment, prevention, and control of NCIP. These guidelines directed case monitoring, reporting, diagnosis, treatment, management, close contact management, and laboratory testing. On January 20, the State Council agreed to include NCIP into the Management of the Infectious Diseases Law and the Health and Quarantine Law. On January 25, the Central Committee of the Communist Party of China set up a leading group to deal with this epidemic.

Epidemic Status

The latest case numbers can be seen on China CDC website: http://114.116.95.250/2019-nCoV/index.html. The geographic distribution and epidemic curve as of January 27, 2020 are shown in Figures 1 and 2.

NCIP in Wuhan continues to spread and the number of cases is still on the rise. The virus has spread to 11 prefectures of Hubei Province outside Wuhan, including Huanggang, Xiaogan, Jingmen, and others.

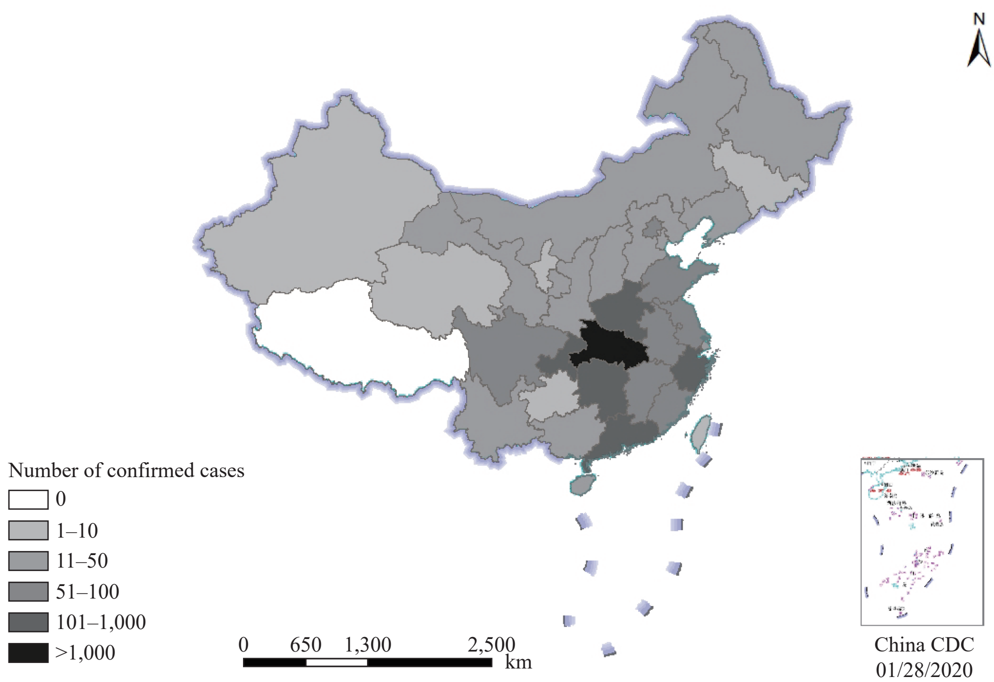

FIGURE 1. The distribution of confirmed cases of 2019 novel coronavirus (2019-nCoV) in China. (as of 24:00 January 27, 2020)

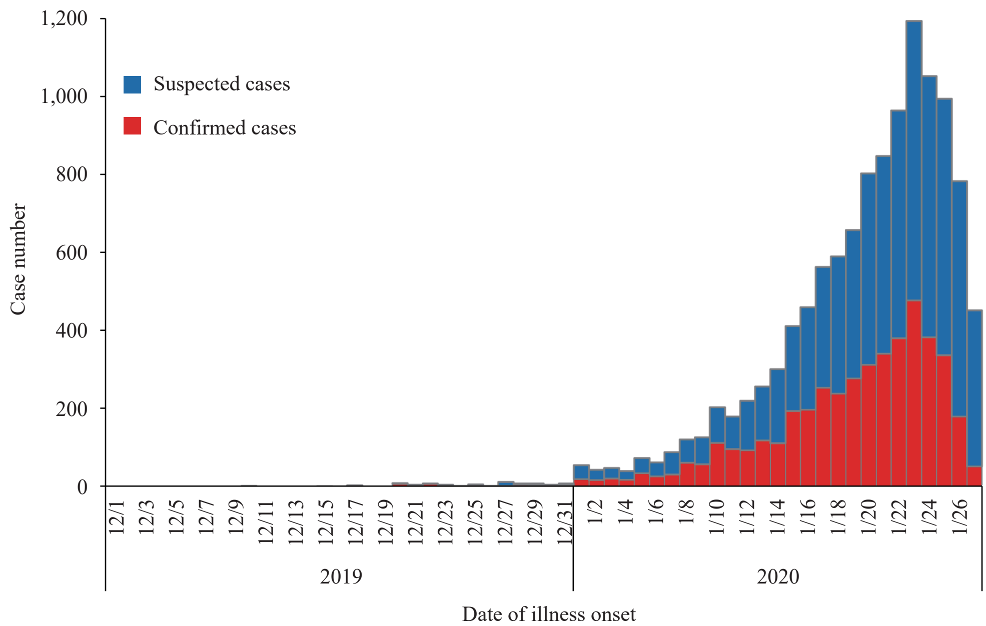

FIGURE 2. Epidemic curve of 2019 novel coronavirus (2019-nCoV) in Mainland China by day. (as of 24:00 January 27, 2020)

Outside of Hubei Province, 29 provinces in Mainland China have reported cases. Currently, most cases are related to Wuhan and others were caused by patients from Wuhan.

Because of the apparent transmission within communities in Wuhan (*3*) and some areas in Hubei Province, mild early symptoms of the disease, and existence of mild cases, diagnosing the disease and quarantining patients in time is difficult and may potentially cause accumulation of infection sources in the community and increase the difficulty in controlling the disease. For this reason, the number of cases in Wuhan and a few other prefectures in Hubei Province may continue to increase.

Most cases in provinces outside of Hubei Province are imported from Wuhan. There has been no apparent transmission within communities in most of those provinces.

Current Key Knowledge of 2019-nCoV

Clinical characteristics of 2019-nCoV can be viewed in the Diagnosis and Treatment Guidelines (*4*). The current male-to-female ratio of all detected cases is 1.2∶1. The median age is 48 years, ranging from 9 months to 96 years, with less than 0.6% of cases under the age of 15 years. The incubation period is approximately 3–7 days. Older patients and patients with underlying diseases are prone to severe illness and death. Nucleic acids from 2019-nCoV have been found in influenza-like illness cases in routine surveillance specimens, and there is some evidence of inapparent infection. The clinical infection spectrums are still under investigation.

The results of the field investigation, laboratory testing, and knowledge of other known coronaviruses indicates that the 2019-nCoV originated in wild animals, even though the host animal(s) are still under investigation. Whether the spillover from animals to humans and the completion of adaptive mutation of the virus occurred in HN market remains to be confirmed, HN market has been identified as the main source of infection for early cases of this epidemic. Current evidence suggests that the main routes of transmission of the virus are through respiratory droplets and close contact. The virus is highly contagious, and its basic reproduction number, i.e. the number cases one infection is suspected to generate, is believed to be between two and three. To date, there is no reliable evidence from field investigations that the disease is contagious during the incubation period.

Public Health Measures

When the preliminary investigation indicated that the epidemic was spreading around the HN market, the market was immediately closed. At the same time, all cases were isolated and treated and close contacts tracked and followed-up with. Environmental samples from the HN market were collected and tested, and case finding, contact tracing, and investigations into the sources of infection were initiated.

Since January 15, suspected cases with travel history to Wuhan were monitored in other regions of China to detect imported cases as early as possible and prevent local transmission. In Wuhan, case surveillance and close contact tracing and management were further strengthened.

Recognizing that 95% of cases detected outside Wuhan were infected during their stay in Wuhan, Wuhan's city buses, subways, ferries, and long-distance passenger transportation were suspended starting on January 23. Citizens of Wuhan were advised not to leave Wuhan without a special reason. Airports and railway stations' departure channels from Wuhan were temporarily closed. All these measures were taken to reduce the bidirectional flow of people. Since January 23, the other 12 prefecture-level cities in Hubei Province have also suspended public transport, stopped activities involving mass gatherings, strengthened community prevention and control, actively detected and diagnosed patients with fever, and strengthened patient admission.

Since January 20, the Chinese Government has launched joint prevention and control mechanisms among 33 central governmental departments, and a series of measures have been taken, including: very frequent media communication and public communication to raise awareness of disease prevention, stopping mass gatherings, encouraging people to reduce personal gatherings and wear face masks to reduce the chance of infection. Cellphone GPS back tracking technology, travelling and visiting history investigations and other measurements have been taken to improve the early detection of cases and reduce spreading.

As of January 25, 30 provinces in China with confirmed cases have launched the highest public health emergency response. China has made great efforts to the community mobilization, which mainly depends on sub-district/township and community/village cadres, primary health care centers and family/village doctors. At the same time, residents and volunteers are encouraged to participate in the full- or part-time working teams engaging in door-to-door health promotion, case detection, and management. Early referral of patients to hospital for medical treatment and management should be ensured to avoid further transmission. Medical doctors and nurses will be mobilized nationwide and deployed to support epidemic center areas, in order to restore normal medical care as soon as possible. The cases will be isolated and treated, and nosocomial infection control will be effectively implemented. In addition, home isolation of mild cases under the guidance of health professionals is encouraged to reduce the burden on the health care system and prevent nosocomial transmission.

Risk Assessment

Current evidence suggests that NCIP has been spreading in humans for more than a month. The main epidemic areas are concentrated in and around Wuhan, and the epidemic is still in its early stage. Authorities at all levels in China have taken strong response measures by mobilizing social forces to promote case detection and management to avoid further transmission, enhancing infection control to avoid outbreaks of nosocomial infection, and encouraging the public to reduce gatherings, travel, and wear masks and to wash hands frequently to reduce exposure and infection opportunities. In Wuhan, vigorous measures have been taken such as suspension of operations for urban buses, the subway, ferries, and long-distance passenger transports, and temporary closure of airports and railway stations. Other prefectures in Hubei Province around Wuhan have also adopted varying degrees of traffic control to restrict the movement and gathering of people. The Chinese Government and people have taken strong and efficient measures to contain this NCIP epidemic, and a larger epidemic, or even pandemic, can be prevented.

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References

1. The 2019-nCoV Outbreak Joint Field Epidemiology Investigation Team, Li Q. An outbreak of NCIP (2019-nCoV) infection in China — Wuhan, Hubei Province, 2019–2020. China CDC Weekly 2020;2(5): 79 – 80. http://weekly.chinacdc.cn/en/article/ccdcw/2020/5/79.
2. Tan WJ, Zhao X, Ma XJ, Wang WL, Niu PH, Xu WB, et al. A novel coronavirus genome identified in a cluster of pneumonia Cases — Wuhan, China 2019–2020. China CDC Weekly 2020;2(4):61 – 2. http://weekly.chinacdc.cn/en/article/ccdcw/2020/4/61.
3. Li Q, Guan XH, Wu P, Wang XY, Zhou L, Tong YQ, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med 2020. http://dx.doi.org/10.1056/NEJMoa2001316.
4. National Health Commission. Diagnosis and treatment guideline on pneumonia infection with 2019 novel coronavirus (the fourth trial edition). http://www.nhc.gov.cn/yzygj/s7653p/202001/4294563ed35b43209b31739bd0785e67.shtml. [2020-1-28]. (In Chinese).

Perspectives

An Estimation of the Total Number of Cases of NCIP (2019-nCoV) — Wuhan, Hubei Province, 2019–2020

Chong You[1]; Qiushi Lin[1]; Xiao-hua Zhou[1,2,#]

Background

On December 31, 2019, the World Health Organization (WHO) was alerted to several cases of pneumonia of unknown etiology in Wuhan, the capital city of Hubei Province in Central China. A novel coronavirus (2019-nCoV) was identified as the causative virus by Chinese authorities on January 7, 2020 (*1*), and China CDC has named the associated disease as novel coronavirus-infected pneumonia (NCIP) (*2–3*). As of January 23, 2020, the National Health Commission (NHC) of China had confirmed a total of 830 cases of NCIP in Mainland China, including 177 in critical condition, 25 fatalities, and 34 recoveries. In Wuhan the origin of the NCIP outbreak, 495 cases including 24 fatalities have been confirmed. In addition to the cases in Mainland China, two cases have been detected in Hong Kong Special Administrative Region, China, two in Macao Special Administrative Region, China, one in Taiwan, China, and a total of nine cases have been detected outside China in Thailand (4 cases), Vietnam (2 cases), USA (1 case), Japan (1 case), Republic of Korea (1 case) and Singapore (1 case) (*4*).

The current epidemiological information has indicated that most of the global cases were directly imported from Wuhan. Therefore, a careful and precise understanding of the total number of cases in Wuhan is crucial for decision making and prevention of NCIP. There has already been a considerable investment of resources in Wuhan in order to combat the spread of NCIP. However, estimating the magnitude of the epidemic in Wuhan based on the reported number of confirmed cases is difficult due to the virus' lengthy incubation period and variable symptom presentation (sometimes without the presence of fever or other symptoms), overburdened medical resources and personnel, and time added to receive test results from China's NHC and China CDC. In this article, a method for estimating the total number of NCIP-onset cases within Wuhan is proposed using the number of cases detected outside Hubei Province.

Results

A total of 3,933 cases of NCIP have been estimated in Wuhan (95% confidence interval [CI]: 3,454–4,450) that had an onset of symptoms by January 19, 2020. The estimate, which uses a statistical model (*5*) of 1,723 cases (95% CI: 427–4,471), was given by another research team on January 12, 2020. Compared with that model (*5*), the existing model is improved by 1) including more data from regions outside Wuhan in the model rather than just the three (now nine) confirmed cases outside China used in that model (*5*), which leads to obtaining a much narrower CI and 2) letting the probability of traveling to region i, namely p_i, be different for different i rather than a constant in that model (*5*), which establishes a more realistic and elaborate model.

Assumptions

The proposed model is based on the following assumptions:

1. Wuhan International Airport has a catchment population of 19 million individuals.

2. There is, on average, a d=10-day window between infection and detection, which includes a 5- to 6-day incubation period and a 4- to 5-day delay from symptom onset to detection.

3. Trip durations are long enough that a traveling patient infected in Wuhan will develop symptoms and be detected in other places rather than after returning to Wuhan.

4. All travelers departing from Wuhan, including transfer passengers, have the same risk of infection as local residents.

5. We only consider symptomatic cases with disease severity of a level that can be detected and do not consider asymptomatic or mild cases.

6. Traveling is independent of the exposure risk to

2019-nCoV or of infection status.

7. Patient recoveries are not considered in the model.

8. The proportion of adjusting for the total passengers by air travel volume is a constant over different regions.

Aside from Assumption 8, the same assumptions were also made in the previous model (*5*). Assumption 7 was not explicitly stated in the previous model (*5*) but is implicitly required. Some of the above assumptions are unrealistic, but the data needed to account for these assumptions are not currently available. The following points are further noted:

(i) Violation of Assumption 2 (e.g., the mean time from infection to detection is longer than 10 days) would cause an overestimation of the total number of cases in Wuhan.

(ii) Violation of Assumption 4 (e.g., travelers have a lower risk of infection than residents in Wuhan) would cause an underestimation.

(iii) Violation of Assumption 6 (e.g., infected individuals are less likely to travel due to the health condition) would cause an underestimation.

(iv) Given that there are very few cases of recovery before January 19, 2020, Assumption 8 should not significantly influence the outcome.

Methods

Table 1 lists the top four regions outside of Hubei Province with a relatively large number of reported confirmed cases alongside the corresponding maximum seating capacity for flights from Wuhan. The number of confirmed cases is positively related to passenger volume from Wuhan. Hence, the following model was considered: the number of imported cases $X_{K+d,i}$ from Wuhan to region i by Day ($K+d$) has a Binomial ($10N_K$, p_i) distribution, $i=1, 2, \cdots, m$, where N_K is the total number of cases in Wuhan by Day K to be estimated, p_i is the daily probability of traveling from Wuhan to region i, which can be estimated using the ratio of daily volume of passengers and the catchment population of Wuhan airport, and d is the mean time from infection to detection (see details of the model explanation in Appendix A). The calculated daily number of travelers based on flight capacity is further described in Appendix B.

TABLE 1. Number of confirmed cases and seating capacity for 4 regions in China.

Region	Total seats	Cases
Guangdong	111,624	53
Zhejiang	46,528	43
Beijing	59,364	26
Shanghai	51,517	20

Determining the number of imported cases in region i, namely $X_{K+d,i}$, plays a crucial role in the modeling procedure. Table 2 shows the number of reported confirmed cases in various provinces/cities/countries (excluding Hubei Province) within and outside of China on January 23, 2020. The column titled "No. of Local Cases" indicates the number of cases which were not directly imported from Wuhan. Despite the rapid spread of the epidemic, the current situation outside Hubei Province is relatively controlled given the adequate medical support being allocated towards the current outbreak. This suggests that the number of reported cases outside Hubei, as of January 23, 2020, is a fairly accurate representation of the actual epidemic situation in the surrounding regions. Note that only cases directly imported from Wuhan were considered. For example, among the 53 confirmed cases reported in Guangdong Province, of which 8 were local cases, the actual number of imported cases, $X_{K+d,i}$, was regarded as 45. Moreover, for the one case in Singapore, the patient departed from the airport in Guangzhou, hence, it was a non-directly imported case and the corresponding $X_{K+d,i}$ is 0. Furthermore, observations from a few nearby provincial-level administrative divisions (PLADs) including Hunan, Anhui, Henan, Jiangxi, and Tibet and other cities within Hubei Province were dropped due to challenges with estimating daily probability of travel without air transportation data from Wuhan.

Using $X_{K+d,i}$ obtained from domestically and internationally reported cases and the corresponding estimated travel probability p_i, where $i=1, 2, \cdots, l$, it is possible to infer the magnitude of comparable cases, N_K, within Wuhan that may have occurred on Day K through a binomial model. The MLE estimate of N_K is 3,933 and the corresponding 95% CI is (3,454–4,450). Note that $X_{K+d,i}$ was obtained on 23 January 2020, hence, the estimated N_K is the number of total cases (including those in incubation period) as of January 14, 2020 or the number of cases with symptom onset by January 19, 2020.

Conclusion

The number of confirmed cases in Wuhan reported by China's NHC has increased rapidly in recent weeks.

TABLE 2. Number of reported confirmed cases within (excluding Hubei) and outside China on 23 January 2020.

Region	No. of cases	No. of local cases
Guangdong	53	8
Zhejiang	43	
Beijing	26	
Shanghai	20	1
Chongqing	27	
Sichuan	15	
Guangxi	13	1
Jiangsu	9	
Shandong	9	1
Hainan	8	
Fujian	5	
Tianjin	4	
Liaoning	4	1
Heilongjiang	4	
Jilin	3	
Shaanxi	3	1
Guizhou	3	1
Ningxia	2	
Xinjiang	2	
Gansu	2	1
Yunnan	1	
Inner Mongolia	1	
Shanxi	1	
Qinghai	0	
Hunan	24	1
Anhui	15	
Henan	9	1
Jiangxi	7	
Hebei	2	
Tibet	0	
Macau, China	2	
Hong Kong, China	2	
Taiwan, China	1	
Japan	1	
South Korea	1	
USA	1	
Thailand	3	
Singapore	1*	
Vietnam	2	1

* The patient was a resident from Wuhan city but departed from the airport in Guangzhou.

However, the currently reported number of 495 cases as of January 23, 2020 in Wuhan is still far below our estimate of 3,933. This may be due to the insufficient amount of medical resources in Wuhan and Hubei Province given the suddenness of the outbreak. We suggest boosting medical resources using specific methods such as increasing the amount of hospital beds in order to accommodate all fever patients with pneumonia or a severe respiratory disease in Wuhan in order to expedite the virus examination process and to allow the region to more adequately respond to this public health crisis.

Appendix A

Assume Day 1 is the date of the infection for the very first case. Let N_j denote the number of cases (including those in incubation period) in Wuhan by Day j, Y_j be the number of the cases traveling to region l on Day i, X_j be the number of cases detected in region l by Day j, p is the pre-defined probability of traveling to region l described in Appendix B and d is the mean time from infection to detection (here we suppress the notation l for conciseness). Then Y_j would follow a binomial distribution listed in Table 3 below. Note that from Day d+1 on, the number of trials in the binomial is no longer N_j but N_j-(N_{j-d}-Y_{j-d}) under Assumption 2. Note that Y_{j-d} is relatively small compare with N_{j-d}, hence we drop Y_{j-d} here for simplicity. Therefore,

$$\sum_{j=1}^{K} Y_j \sim Binomial\left(\sum_{j=K-d+1}^{K} N_j, p\right), K > d \quad (1)$$

However, note that Y_j would not be directly observed on Day j or any other single day but would be detected between a certain period listed in Table 1. For example, suppose that N_K is of interest, then $\sum_{i=1}^{K} Y_i$ needs to be calculated, note that $Y_1,\cdots,Y_K$ would be all included in X_{K+d}, but $\sum_{i=1}^{K} Y_i \leq X_{K+d}$ as the observed X_K would include parts of $Y_{K+1},\cdots,Y_{K+d-1}$. A straightforward but rough way to approximate $\sum_{i=1}^{K} Y_i$ is to use $X_{K+d/2}$. The other problem is that using such binomial model, what we can estimate is $\sum_{i=K-d+1}^{K} N_i$ but not a single N_i, we suggest using $\sum_{i=K-d+1}^{K} N_i/\mathrm{d}$ as an estimation of $N_{K-d/2}$, that is

$$X_{K+d/2} \sim Binomial\left(d \times N_{K-d/2}, p\right), \quad K > d \quad (2)$$

A binomial distribution can be approximated by a Poisson distribution if the number of trials in the binomial distribution is large while the probability of success is small. Hence,

$$X_{K+d} \approx Poisson\left(d \times p \times N_K\right), \quad K > d/2 \quad (3)$$

TABLE 3. Binomial distributions on Day *i*.

Date	Distribution	Period of Y_i being detected
Day 1	Y_1~Binomial(N_1,p)	Y_1 is expected to be detected on Day d+1
Day 2	Y_2~Binomial(N_2,p)	Y_2 is expected to be detected on Day d+1 and Day d+2
⋮	⋮	⋮
Day d	Y_d~Binomial(N_d,p)	Y_d is expected to be detected between Day d+1 and Day 2d
Day d+1	Y_{d+1}~Binomial(N_{d+1}−N_1,p)	Y_{d+1} is expected to be detected between Day d+2 and Day 2d+1
⋮	⋮	⋮
Day 2d−1	Y_{2d-1}~Binomial(N_{2d-1}−N_{d-1},p)	Y_{2d-1} is expected to be detected between Day 2d and Day 3d−1
Day 2d	Y_{2d}~Binomial(N_{2d}-N_d,p)	Y_{2d} is expected to be detected between Day 2d+1 and Day 3d

Including multiple regions into the model, we have

$$X_{K+d,i} \approx Poisson\left(d \times p_i \times N_K\right) \quad \text{for } i = 1, 2, \cdots, m, \tag{4}$$

and therefore,

$$\sum_{i=1}^{m} X_{K+d,i} \sim Poisson\left(d \times N_K \sum_{i=1}^{m} p_i\right) \tag{5}$$

where m=25 is the total number of regions used in our model. Note that if p_i=p, our model is almost identical to the previous model (*5*). The total number of cases on Day K, N_K, is estimated by its maximum likelihood estimate (MLE), that is

$$\hat{N}_K = \frac{\sum_{i=1}^{m} X_{K+d,i}}{d \times \sum_{i=1}^{m} P_i} \tag{6}$$

and the corresponding (1−α) CI is derived using the relation between Poisson distribution and chi-square distribution (*6*).

$$\left(\frac{\chi^2_{2(\sum_{i=1}^{m} X_{K+d,i}),\alpha/2}}{2 \times d\sum_{i=1}^{m} p_i}, \frac{\chi^2_{2(\sum_{i=1}^{m} X_{K+d,i})+2,1-\alpha/2}}{2 \times d\sum_{i=1}^{m} p_i}\right) \tag{7}$$

Appendix B

The daily probability of traveling from Wuhan to region i, p_i, can be estimated using the ratio of daily volume of passengers to region i and the catchment population of Wuhan airport. Below are the details for obtaining daily volume of passengers to region i.

There were a total of 7,122 flights from Wuhan to 84 airports in Mainland China in the 30 days from December 22, 2019 to January 20, 2020, where 6,586 flights were to the top 50 destinations which accounted for 6,586/7,122=92.47% of the total volume (*7*). Meanwhile, there were 854,383 seats in the flights to top 50 destinations being reported in IATA data in the 22 days between December 30, 2019 and January 20, 2020 (*8*). Hence, the average number of seats in a single flight can be estimated by 854,383/(6,586×22/30)=177. Over Spring Festival/Lunar New Year, Wuhan airport is expected to handle 24,600 flights and 3.52 million passengers in 40 days (*9*), and thus, each flight is expected to have on average 3,520/24.6=143 passengers onboard, which gives an average load factor of a flight departing from Wuhan as 143/177=0.81. Therefore, the total volume of air travels during the Spring Festival/Lunar New Year can be estimated to be 854,383×0.81/0.9274/22×40=1.35 million. In addition, based on historical evidence, 15 million passengers are expected to depart Wuhan by rail, road, and air, 66% of whom are estimate to travel across 300 km (*10*). That would imply, on average, that 135/(1,500×0.34)=26.47% of trips longer than 300 km would be by air. Therefore, the total passenger volume from Wuhan to other regions in Mainland China can be calculated by *the number of seats*×0.81/0.2647. Note that Hainan Province is a special case because of its geographical location, and a majority of passengers from Wuhan to Hainan Province will likely travel by air. As a result, we would use *the number of seats* ×0.81 for Hainan Province. For other international regions, we use the estimate of 3,301 passengers per day given by the previous model (*5*).

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References

1. Novel Coronavirus (2019-nCoV). World Health Organization WHO 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019. [2020-1-24].
2. Tan WJ, Zhao X, Ma XJ, Wang WL, Niu PH, Xu WB, et al. A novel coronavirus genome identified in a cluster of pneumonia cases — Wuhan, China 2019–2020. China CDC Weekly 2020;2(4):61–2. http://weekly.chinacdc.cn/en/article/ccdcw/2020/4/61.
3. The 2019-nCoV Outbreak Joint Field Epidemiology Investigation Team, Li Q. An outbreak of NCIP (2019-nCoV) infection in China —

Wuhan, Hubei Province, 2019-2020. China CDC Weekly 2020; 2(5):79–80. http://weekly.chinacdc.cn/en/article/ccdcw/2020/5/79.
4. The current outbreak of novel coronavirus pneumonia on 24 January. National Health Commission of the People's Republic of China. http://www.nhc.gov.cn/yjb/s3578/202001/c5da49c4c5bf4bcfb320ec2036480627.shtml. [2020-1-24] (In Chinese).
5. Natsuko Imai, Ilaria Dorigatti, Anne Cori, Steven Riley, Neil M. Estimating the potential total number of novel coronavirus cases in Wuhan City, China. Imperial College London 2020;1-4. https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/2019-nCoV-outbreak-report-17-01-2020.pdf.
6. Ulm K. Simple method to calculate the confidence interval of a standardized mortality ratio. Am J Epidemiol 1990;131(2):373–5. https://doi.org/10.1093/oxfordjournals.aje.a115507.
7. Zhu J. Where might the novel coronavirus has moved before the closure? A forecast based on migration + air + rail data forecast. Urban Data Party https://mp.weixin.qq.com/s/OL_0FZKLFcBXrEvQq28d-A. [2020-1-24] (In Chinese).
8. Where have the residents of Wuhan been in these 22 days of outbreak of novel coronavirus pneumonia? https://mp.weixin.qq.com/s/7ynWYxB-s7nfz7rmjBLSpQ. [2020-1-24] (In Chinese).
9. Wuhan Tianhe airport is expected to handle 3.52 million passengers over the Chinese New Year travel rush. Chutian Metropolis Daily http://www.ctdsb.net/html/2020/0110/hubei284612.html. [2020-1-24] (In Chinese).
10. Big data perspective: Wuhan in the Chinese New Year travel rush. Daily economic news https://m.nbd.com.cn/articles/2020-01-22/1402239.html. [2020-1-24] (In Chinese).

Commentary

Beating Neglected Tropical Diseases: For Good and For All

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The term neglected tropical diseases (NTDs) was coined about 15 years ago because this group of diseases is predominantly endemic in tropical and subtropical areas and neglected in research and control compared to HIV/AIDS, tuberculosis, and malaria (*1*–*2*). Thus, compared to the early establishment of World Days for "the big three diseases", namely HIV/AIDS, tuberculosis, and malaria in 1988, 1995, and 2007, respectively, Jan 30, 2020 has just designated as the first World NTDs Day with the slogan of "Beat NTDs: For good. For all" (*3*).

A group of 20 diseases, most of which are infectious diseases, are included in World Health Organization's NTDs list (*4*), but several other diseases are also classified as NTDs in the Global Burden of Diseases Study (*5*). On the one hand, NTDs cause a high burden of disease at an estimated 17 million disability-adjusted life years (DALYs) in 2017 (*5*). On the other hand, most of the burden occurs disproportionally in less developed areas. Over 80% of the DALYs (14 million) in 2017 were distributed in sub-Saharan Africa, South Asia, Southeast Asia, and Latin America and Caribbean (*5*), and NTDs predominantly affect marginalized communities and populations there.

Many determinants drive the endemicity and persistence of NTDs. Affected populations usually live in poor natural environments, which favor the survival of causative agents. Inadequate infrastructure, especially unavailability of clean water and sanitation, promotes the transmission of NTDs. Less economic development leads to high dependence on traditional and low-level animal husbandry, which results in the transmission of many zoonotic NTDs. Unfavorable natural environments and poor economies hinder adequate access to medical resources for diagnosis, treatment, and control. These determinants are all directly and indirectly related to poverty. In addition, endemicity of NTDs there worsens the poverty due to medical cost and loss of productivity and husbandry. Thus, poverty and NTDs establish a vicious cycle, while poverty reduction and control of NTDs have to promote each other mutually (*6*).

A distinguished example of mutual promotion between poverty reduction and control of NTDs has been demonstrated in China. At least 11 NTDs have exerted a huge disease burden in China historically (*7*). For example in the 1950s, over 50% of the population was affected by trachoma, 31.0 million by lymphatic filariasis, 11.6 million by schistosomiasis, 530,000 by visceral leishmaniasis, and a major population by intestinal helminthiases. Then, lymphatic filariasis was declared eliminated as a public health problem in 2007 followed by trachoma in 2015 (*7*). Cases of schistosomiasis decreased to 37,600 in 2017 and is targeted to be nationally eliminated by 2030. Meanwhile, only several hundred visceral leishmaniasis cases occur each year. The cases with soil-transmitted helminthiases had decreased from 646 million in the early 1990s to 29 million in 2015 and is continuing to decrease (*7*–*8*).

The control of NTDs in China steps synchronously with poverty reduction. Since the economic reform and opening up in 1978, the population living under the poverty line has been drastically reduced by over 700 million in China (*9*). Developed areas in eastern regions of China also show effective control and elimination of many NTDs, while less developed areas in western regions of China are still prevalent with some NTDs. In 2015, the central government called for poverty eradication by 2020 in China (*10*). By 2018, the poverty rate had decreased to 1.7%, namely a total number of 16.6 million (*9*), and significant effort is being made to reach the target of zero poverty by 2020. Right now, western areas with a high burden of NTDs are prioritized in the national poverty eradication program. So as further control and elimination of NTDs is promising in China, and will consolidate the achievements of poverty eradication. China has contributed greatly to both global poverty reduction and NTD control as indicators set by the United Nations Sustainable Development Goals (SDGs) (*11*).

The establishment of World NTDs Day demonstrates global willingness to combat NTDs by further promoting awareness of NTDs and subsequent input of resources to control NTDs. The strong mutually causal relationship between poverty and NTDs implies high dependence on poverty reduction to combat NTDs and high contribution by the latter to the former. Global control of NTDs impacts the achievement of universal health coverage due to the huge population affected and high burden exerted. During this progress, universal coverage of poverty reduction will be of crucial importance. Both poverty reduction and NTD control need international cooperation to ultimately achieve the United Nations SDGs (*11*). The Belt and Road Initiative is such a cooperative platform for the global fight against both poverty and NTDs (*12*).

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References

1. Molyneux DH. “Neglected” diseases but unrecognised successes--challenges and opportunities for infectious disease control. Lancet 2004;364(9431):380 – 3. http://dx.doi.org/10.1016/S0140-6736(04)16728-7.
2. Molyneux DH, Savioli L, Engels D. Neglected tropical diseases: progress towards addressing the chronic pandemic. Lancet 2017;389(10066):312 – 25. http://dx.doi.org/10.1016/S0140-6736(16)30171-4.
3. 2020: a crucial year for neglected tropical diseases. Lancet 2019;394(10215):2126. http://dx.doi.org/10.1016/S0140-6736(19)33070-3.
4. World Health Organization. Neglected tropical diseases. https://www.who.int/neglected_diseases/diseases/en/.[2020-1-24].
5. Global Burden of Disease Study 2017. Global Burden of Disease Study 2017 (GBD 2017) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2018. http://vizhub.healthdata.org/gbd-compare/.[2020-1-24].
6. Hotez PJ. Whatever happened to China’s neglected tropical diseases?. Infect Dis Poverty 2019;8(1):85. http://dx.doi.org/10.1186/s40249-019-0598-5.
7. Qian MB, Chen J, Bergquist R, Li ZJ, Li SZ, Xiao N, et al. Neglected tropical diseases in the People’s Republic of China: progress towards elimination. Infect Dis Poverty 2019;8(1):86. http://dx.doi.org/10.1186/s40249-019-0599-4.
8. Zhu HH, Huang JL, Zhou CH, Zhu TJ, Qian MB, Zhang MZ, et al. Soil-transmitted helminthiasis — China, 2018. China CDC Weekly 2020;2(3):34-8. http://weekly.chinacdc.cn/en/article/ccdcw/2020/3/34.
9. National bureau of statistics of the People’s Republic of China. China Statistical Yearbook 2019. http://www.stats.gov.cn/tjsj/ndsj/2019/indexeh.htm.[2020-1-24].
10. State Council of the People’s Republic of China. Poverty alleviation plan for the 13th Five-Year Plan period (2016-2020). http://www.gov.cn/zhengce/content/2016-12/02/content_5142197.htm.[2020-1-24].
11. United Nations. Sustainable Development Goals. https://www.un.org/sustainabledevelopment/sustainable-development-goals/.[2020-1-29].
12. Chen J, Bergquist R, Zhou XN, Xue JB, Qian MB. Combating infectious disease epidemics through China’s Belt and Road Initiative. PLoS Negl Trop Dis 2019;13(4):e0007107. http://dx.doi.org/10.1371/journal.pntd.0007107.

Notifiable Infectious Diseases Reports

Reported Cases and Deaths of National Notifiable Infectious Diseases — China, December, 2019

Diseases	Cases	Deaths
Plague	0	0
Cholera	0	0
SARS-CoV	0	0
Acquired immune deficiency syndrome	6,735	2,284
Hepatitis	126,743	54
Hepatitis A	1,316	1
Hepatitis B	102,151	43
Hepatitis C	20,327	7
Hepatitis D	43	0
Hepatitis E	1,888	1
Other hepatitis	1,018	2
Poliomyelitis	0	0
Human infection with H5N1 virus	0	0
Measles	230	0
Hemorrhagic fever with renal syndrome	1,364	7
Rabies	19	30
Japanese encephalitis	12	1
Dengue	268	0
Anthrax	24	0
Dysentery	3,970	0
Tuberculosis	71,631	230
Typhoid fever and paratyphoid fever	571	0
Meningococcal meningitis	15	1
Pertussis	1,414	1
Diphtheria	0	0
Neonatal tetanus	3	0
Scarlet fever	13,053	0
Brucellosis	3,065	1
Gonorrhea	10,803	0
Syphilis	48,587	4
Leptospirosis	16	1
Schistosomiasis	12	0
Malaria	204	4
Human infection with H7N9 virus	0	0
Influenza	1,199,771	16
Mumps	27,581	0
Rubella	1,718	0

Continued

Diseases	Cases	Deaths
Acute hemorrhagic conjunctivitis	3,046	0
Leprosy	43	0
Typhus	63	0
Kala azar	11	0
Echinococcosis	381	0
Filariasis	0	0
Infectious diarrhea*	122,103	1
Hand, foot and mouth disease	63,866	0
Total	**1,707,322**	**2,635**

* Infectious diarrhea excludes cholera, dysentery, typhoid fever and paratyphoid fever.

The number of cases and cause-specific deaths refer to data recorded in National Notifiable Disease Reporting System in China, which includes both clinically-diagnosed cases and laboratory-confirmed cases. Only reported cases of the 31 provincial-level administrative divisions in Mainland China are included in the table, whereas data of Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan are not included. Monthly statistics are calculated without annual verification, which were usually conducted in February of the next year for de-duplication and verification of reported cases in annual statistics. Therefore, 12-month cases could not be added together directly to calculate the cumulative cases because the individual information might be verified via National Notifiable Disease Reporting System according to information verification or field investigations by local CDCs.

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