Original research

Effect of public health interventions on COVID-19 cases: an observational study

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ABSTRACT

Background As the epidemic of COVID-19 is gradually controlled in China, a summary of epidemiological characteristics and interventions may help control its global spread.

Methods Data for COVID-19 cases in Hubei Province (capital, Wuhan) was extracted until 7 March 2020. The spatiotemporal distribution of the epidemic in four periods (before 10 January, 10–22 January, 23 January–6 February and 7 February–7 March) was evaluated, and the impacts of interventions were observed.

Results Among 67 706 COVID-19 cases, 52 111 (76.97%) were aged 30–69 years old, and 34 680 (51.22%) were women. The average daily attack rates (95% CI) were 0.5 (0.3 to 0.7), 14.2 (13.2 to 15.1), 45.7 (44.0 to 47.5) and 8.6 (7.8 to 9.3) cases per 10^6 people in four periods, and the harmonic means (95% CI) of doubling times were 4.28 (4.01 to 4.55), 3.87 (3.78 to 3.98), 5.40 (4.83 to 6.05) and 45.56 (39.70 to 52.80) days. Compared with the first period, daily attack rates rose rapidly in the second period. In the third period, 14 days after 23 January, the daily average attack rate in and outside Wuhan declined by 33.8% and 48.0%; the doubling times increased by 95.0% and 133.2%. In the four periods, 14 days after 7 February, the daily average attack rate in and outside Wuhan decreased by 79.1% and 95.2%; the doubling times increased by 79.2% and 152.0%.

Conclusions The public health interventions were associated with a reduction in COVID-19 cases in Hubei Province, especially in districts outside of Wuhan.

Key messages

What is the key question?

► Since the outbreak, the full spectrum of the outbreak and the impact of non-pharmaceutical interventions on COVID-19 in Hubei Province are still unclear.

What is the bottom line?

► We analysed the effects of non-pharmaceutical intervention measures, including district traffic interruption, wearing masks in public places and isolating infected patients and close contacts, on stopping the epidemic in Wuhan and Hubei Province (except for Wuhan) among 67 706 COVID-19 cases and found that the effects of these preventive measures were timely and obvious.

Why read on?

► We believe that the findings could help provide a relatively comprehensive understanding of epidemiological characteristics and intervention measures of COVID-19 and similar infectious diseases.

INTRODUCTION

COVID-19, a novel coronavirus disease caused by SARS-CoV-2, was first reported in December 2019 in Wuhan, Hubei Province, China.[1] Due to the infectious nature of this disease, an increasing number of cases have been reported in multiple countries since the beginning of 2020. The WHO declared the outbreak of COVID-19 as a Public Health Emergency of International Concern on 30 January 2020 and announced a global pandemic of COVID-19 on 11 March 2020. As of 18 April 2020, a total of 2 160 207 COVID-19 cases and 146 088 deaths have been reported worldwide[2]; more than 82 000 cases in China have been confirmed, of which 4632 patients have died.[3] The COVID-19 epidemic has caused emergency responses in many countries and regions around the world.

Hubei is the first province in China to report COVID-19 cases and is also the province with the highest number of cases, accounting for more than 80% of the total confirmed cases and more than 95% of the total deaths of China.[3] On 23 January 2020, 70 new daily cases of COVID-19 were reported in Wuhan, the capital of Hubei Province.[4] The government took measures to suspend all traffic connections of Wuhan and to block the roads out of Wuhan. In the following 4 days, all 17 districts and surrounding counties in Hubei Province implemented interruption and isolation measures. Although the number of daily reported new cases increased to 14 840 on 12 February,[5] it started to decrease after that, reaching 1807 cases on 17 February[6] in Hubei Province. After effective non-pharmaceutical interventions, the epidemic situation of COVID-19 in Hubei has been controlled. As of 7 March, the number of daily newly confirmed cases of COVID-19 in Hubei Province was less than 50.[7] Since the outbreak, clinical and epidemiological characteristics of COVID-19 have been partially reported,[8–11] though the full spectrum of the outbreak and impact of non-pharmaceutical interventions on COVID-19 in Hubei Province are still unclear.

Therefore, we conducted this study to describe the epidemiological characteristics and transmission model of COVID-19 in Hubei Province according to individual data for 67 706 cases from the Provincial Notifiable Disease Report System. We divided the epidemic into four periods and compared epidemiological characteristics across these periods. The role and effectiveness of intervention measures in controlling the spread and new onset of disease were evaluated by analysing changes in the number of daily new cases, attack rate, spatial clustering and doubling times of cases in the different periods.

METHODS

Source of COVID-19 case data

COVID-19 case data for Hubei Province up until 7 March 2020 were extracted from the Provincial Notifiable Disease Report System. All data were incorporated into this analysis after removing personal identification information. We collected demographic characteristics for cases including age, sex, occupation, report district, date of illness onset (the date of self-reported symptoms such as fever, cough and/or other respiratory symptoms), date of confirmed diagnosis (laboratory-confirmed date or clinically diagnosed date) and contact history.

Case definitions

COVID-19 cases included laboratory-confirmed cases and clinically diagnosed cases. According to the *Diagnosis and Treatment Scheme for COVID-19* released by the National Health Commission of China,[12] a laboratory-confirmed case was defined if the patient had a fever, cough and/or other respiratory symptoms, clear epidemiological history and a positive laboratory test of SARS-CoV-2. A clinically diagnosed case was defined as having consistent clinical symptoms, epidemiological history and CT imaging characteristics with coronavirus pneumonia. We collected clinically diagnosed cases because of the lack of laboratory testing capability and the many cases in the early stage during the outbreak. Before 5 February 2020, the cases included patients diagnosed clinically and/or by laboratory testing, whereas from then on, the laboratory detection ability improved,[13] and all cases were laboratory confirmed. The severity status was categorised as mild, common, severe and critical based on the *scheme*. In the ensuing analysis, we combined laboratory-confirmed cases and clinically diagnosed cases. Clustered cases were defined as the occurrence of two or more cases of fever and/or respiratory symptoms in a small area such as home, office, school or class within 2 weeks.

Source of data for each district in Hubei Province

Basic information of the 17 districts of Hubei Province in 2018 was obtained from the Hubei Provincial Government website (http://www.hubei.gov.cn/). The migration rate and travel intensity for each district were extracted from Baidu migration (http://qianxi.baidu.com/). The migration rate is defined as the average population rate for Wuhan residents travelling to a certain district in Hubei. Travel intensity is defined as the ratio of the average number of people travelling in the district to the total resident population.

Selection of important time points to reflect the epidemic trends and effectiveness of relevant interventions

To better reflect the epidemic trends of COVID-19 and the effectiveness of relevant interventions, we divided the outbreak into four periods based on the important dates that may affect the spread of the virus.[14] 10 January 2020, the first date of the largest population movement before the Spring Festival, was considered the first time point when interdistrict migration increased dramatically and was expected to accelerate the spread of COVID-19. The second time point was 23 January, when the Wuhan municipal government blocked all out-of-district transportation, with the other districts in Hubei Province following up within 4 days. The third time point was 7 February, when centralised treatment and the isolation of 'four types of personnel' were completed basically in Hubei Province. The four types of personnel are confirmed cases, suspected cases, cases with a fever that cannot be ruled out and close contacts of COVID-19 cases. To assess the spatiotemporal distribution trend and impact of non-pharmaceutical interventions of the epidemic, we calculated the cumulative number of cases and cumulative attack rate for COVID-19 from case 0 up to 1 day before the above three time points and the last day (7 March 2020). We also divided the COVID-19 outbreak into four periods (before 10 January, 10–22 January, 23 January–6 February and 7 February–7 March 2020) and calculated the daily average number of cases and daily average attack rate in the four periods.

Statistical analysis

The demographic and epidemiological characteristics of COVID-19 cases were analysed by descriptive statistics. An epidemic curve was drawn based on the daily number of cases (Y-axis) and the onset date (X-axis). The daily attack rate was defined as the number of COVID-19 cases per day per 10^6 people ($/10^6$). To carry out spatiotemporal analysis, the district location of each case at the time of onset was used to draw a colour map. A Wilcoxon signed-rank test was used to compare the average daily new cases and attack rates of COVID-19 between in and outside Wuhan in different periods. The global spatial autocorrelation of COVID-19 attack rates was explored by Moran's *I* test. Local Indicators of Spatial Association were generated to determine the location of spatial clusters of districts with similar COVID-19 attack rates. 'High-high gathering' indicates high attack rate at observation city and high attack rate around; 'low-low gathering' indicates low attack rate at observation city and low attack rate around; 'High-low gathering' indicates high attack rate at observation city but low attack rate around; 'low-high gathering' indicates low attack rate at observation city but high attack rate around. We also calculated the doubling times of COVID-19 onset cases,[15] as follows:

$$\alpha(t) = t\ln(2)/\ln(N/N_0)$$

where α is doubling times; t is the time, which is reset to 0 at N_0; N is the total cases; and N_0 is the initial total cases, which is chosen as the cumulative number of cases on the first day of each period.

To quantify parameter uncertainty of doubling times, we used parametric bootstrapping with a Poisson error structure around the harmonic mean of doubling times to obtain the 95% CI.[16]

All of the analyses were performed using R V.3.63, Microsoft Office 2019 and GeoDa spatial analytic software (http://geodacenter.github.io/download.html).

RESULTS

General characteristics of districts in Hubei Province

Hubei Province has 17 districts, with a permanent resident population of 59.17 million. Wuhan is the capital of Hubei Province; it had a permanent population of 11.08 million and a per capita gross domestic product of 133 988.76 yuan in 2018. Between 1 and 23 January, approximately 66.74% of the total floating population of Wuhan travelled to other districts in Hubei

Table 1 General situation of each district in Hubei Province

	Total area (km²)	Population of permanent residents (10 000 persons)	Per capital GDP (yuan)	Migration rate* (%)	Travel intensity in the district†	Date of cordon sanitaire around the district	Total COVID-19 cases
Wuhan	8494	1108.10	133 988.76	-–	4.66	23 January 2020	49 912
Huangshi	4586	247.07	64 246.27	3.81	5.35	24 January 2020	1015
Shiyan	23 680	340.60	51 315.99	1.84	5.20	25 January 2020	672
Jingzhou	14 067	559.02	37 247.03	6.09	4.99	24 January 2020	1580
Yichang	21 084	413.59	98 267.11	2.75	5.30	25 January 2020	931
Xiangyang	19 724	566.90	76 023.77	3.87	5.16	27 January 2020	1175
Ezhou	1596	107.77	93 281.99	4.48	4.33	23 January 2020	1393
Jingmen	12 404	289.65	63 797.34	3.01	5.29	24 January 2020	928
Huanggang	17 457	633.00	32 151.70	12.20	5.07	24 January 2020	2907
Xiaogan	8910	492.00	38 879.98	12.92	4.90	25 January 2020	3518
Xianning	10 049	254.33	53 568.88	5.14	5.62	24 January 2020	836
Xiantao	2538	114.00	70 186.84	2.71	4.61	23 January 2020	575
Qianjiang	2004	96.60	78 238.10	1.14	4.64	23 January 2020	198
Shennongjia	3253	7.67	37 275.10	0.17	4.57	25 January 2020	11
Enshi Tujia and Miao	24 111	337.80	25 783.01	1.84	5.50	26 January 2020	252
Tianmen	2622	127.23	46 463.10	1.84	5.25	24 January 2020	496
Suizhou	9636	221.67	45 616.69	2.93	4.88	25 January 2020	1307

*The migration rate is the mean of data from 1 to 23 January 2020.
†Travel intensity is the mean of data between 1 January 2020 and the date of blocking traffic connections.
GDP, gross domestic product.;

Province, among which Xiaogan and Huanggang were the top two, with migration rates of 12.92% and 12.20%, respectively (table 1).

General characteristics of COVID-19 cases

A total of 67 706 cases were incorporated in our analysis, of which 52 111 (76.97%) were aged 30–69 years old. Nearly half of the patients (n=33 026, 48.78%) involved male patients; 80.51% of the patients (n=54 512) were mild or common in clinical severity. Only 18.57% (n=12 573) of patients reported having contact with COVID-19 case(s), and 10.15% (n=6872) were clustered cases (table 2).

The epidemic curve based on the onset date and important intervention measures is shown in figure 1. The average daily onset number of cases was at a low level in December 2019. On 10 January 2020, the number of daily new cases was 225. After that, the number rose rapidly to 2779 on 23 January and peaked at 4433 on 1 February. It then gradually declined to 1695 cases on 7 February and finally to one case on 7 March. A similar trend was found in Wuhan, but the trend was more moderate in Hubei Province (except for Wuhan), especially between 10 and 23 January.

The onset situation and daily attack rates ($/10^6$) of Hubei Province, Hubei Province (except for Wuhan), and the 17 districts are shown in figure 2. The first onset of COVID-19 in Wuhan was on 8 December 2019, and the first onset in Suizhou, Tianmen and Xiaogan was on 10, 18 and 21 December, respectively. On 17 January 2020, COVID-19 appeared in the last district of Hubei Province, Shennongjia mountain district. The highest daily attack rates of Hubei Province (74.9 cases $/10^6$) and Hubei Province (except for Wuhan) (21.5 cases $/10^6$) appeared on 1 February 2020. On the same day, Wuhan had the highest daily attack rate ($/10^6$), with 306.6 cases, followed by Ezhou, Xiaogan and Suizhou, with 72.4, 48.0 and 44.7 cases, respectively. The total attack rate ($/10^6$) in Hubei Province, Hubei Province (except for Wuhan) and Wuhan was 1144.3, 370.0 and 4504.3 cases, respectively.

Spatiotemporal distribution and effect of non-pharmaceutical interventions of COVID-19 cases

The spatiotemporal distribution of the cumulative number of cases and attack rates of COVID-19 at four time points (9 January, 22 January, 6 February and 7 March 2020) is shown in figure 3. Except for Wuhan (914 cases) and Xiaogan (12 cases), there were no more than 10 cases in other districts as of 9 January. The cumulative cases exceeded 500 in Wuhan and Xiaogan districts and between 100 and 500 in 11 other districts until 22 January. As of 6 February, the cumulative number of cases exceeded 1000 cases in six districts, namely Wuhan (37 344 cases), Xiaogan (3036 cases), Huanggang (2428 cases), Jingzhou (1366 cases), Suizhou (1144 cases), Ezhou (1099 cases) and Xiangyang (1046 cases). The cumulative numbers of cases in adjacent Wuhan districts and non-adjacent Wuhan districts were 9987 and 5134, respectively. Compared with 6 February, the cumulative number of cases on 7 March had increased, but the speed of increase was relatively gradual (figure 3A). Similar trends were observed for the cumulative attack rate in the four periods (figure 3B).

Daily new cases during the study periods are depicted in figure 1 figure 4, and daily attack rates ($/10^6$) of COVID-9 in figures 2 and 4B. The average numbers of daily new cases for Hubei Province in the four periods were 29.7, 838.2, 2705.9 and 508.0, for Hubei Province (except for Wuhan) were 2.0, 228.8, 805.3 and 89.1, and for Wuhan were 27.7, 609.4, 1900.5 and 418.9, respectively. The daily average attack rates ($/10^6$) (95% CI) for Hubei Province in the four periods were 0.5 (0.3 to 0.7), 14.2 (13.2 to 15.1), 45.7 (44.0 to 47.5) and 8.6 (7.8 to

Table 2 Characteristic of COVID-19 cases in Hubei Province (n=67 706)

	Total (n (%))	Before 10 January (n (%))	10–22 January (n (%))	23 January–6 February (n (%))	7 February–7 March (n (%))
No	67 706	980	10 897	40 588	15 241
Type					
Confirmed case	48 944 (72.29)	610 (62.24)	7944 (72.9)	30 262 (74.56)	10 128 (66.45)
Clinically diagnosed cases	18 762 (27.71)	370 (37.76)	2953 (27.1)	10 326 (25.44)	5113 (33.55)
Age					
0~	619 (0.91)	1 (0.1)	16 (0.15)	196 (0.48)	406 (2.66)
10~	662 (0.98)	1 (0.1)	37 (0.34)	288 (0.71)	336 (2.2)
20~	4507 (6.66)	36 (3.67)	679 (6.23)	2611 (6.43)	1181 (7.75)
30~	10 147 (14.99)	86 (8.78)	1661 (15.24)	6182 (15.23)	2218 (14.55)
40~	12 009 (17.74)	139 (14.18)	1946 (17.86)	7338 (18.08)	2586 (16.97)
50~	15 392 (22.73)	254 (25.92)	2636 (24.19)	9444 (23.27)	3058 (20.06)
60~	14 563 (21.51)	267 (27.24)	2524 (23.16)	8869 (21.85)	2903 (19.05)
70~	6884 (10.17)	142 (14.49)	1037 (9.52)	4138 (10.2)	1567 (10.28)
≥80	2923 (4.32)	54 (5.51)	361 (3.31)	1522 (3.75)	986 (6.47)
Gender					
Male	33 026 (48.78)	492 (50.2)	5298 (48.62)	20 016 (49.32)	7220 (47.37)
Female	34 680 (51.22)	488 (49.8)	5599 (51.38)	20 572 (50.68)	8021 (52.63)
Occupation					
Service	4775 (7.05)	68 (6.94)	880 (8.08)	3100 (7.64)	727 (4.77)
Farmer/worker	10 483 (15.48)	60 (6.12)	1496 (13.73)	6767 (16.67)	2160 (14.17)
Medical personnel	3019 (4.46)	36 (3.67)	745 (6.84)	1763 (4.34)	475 (3.12)
Retiree	17 069 (25.21)	325 (33.16)	2880 (26.43)	10 441 (25.72)	3423 (22.46)
Others	20 661 (30.52)	337 (34.39)	3431 (31.49)	11 363 (28)	5530 (36.28)
Unknown	11 699 (17.28)	154 (15.71)	1465 (13.44)	7154 (17.63)	2926 (19.2)
Disease severity					
Mild	31 098 (45.93)	188 (19.18)	3662 (33.61)	20 145 (49.63)	7103 (46.6)
Common	23 414 (34.58)	316 (32.24)	4016 (36.85)	12 803 (31.54)	6279 (41.2)
Severe	10 542 (15.57)	257 (26.22)	2497 (22.91)	6256 (15.41)	1532 (10.05)
Critical	2195 (3.24)	95 (9.69)	560 (5.14)	1264 (3.11)	276 (1.81)
Missing value	457 (0.67)	124 (12.65)	162 (1.49)	120 (0.3)	51 (0.33)
Days from illness to diagnosis					
<10	35 734 (52.78)	0 (0)	1816 (16.67)	20 630 (50.83)	13 288 (87.19)
10~	23 787 (35.13)	191 (19.49)	4729 (43.4)	16 998 (41.88)	1869 (12.26)
20~	6379 (9.42)	165 (16.84)	3531 (32.4)	2599 (6.4)	84 (0.55)
30~	1440 (2.13)	370 (37.76)	730 (6.7)	340 (0.84)	0 (0)
≥40	366 (0.54)	254 (25.92)	91 (0.84)	21 (0.05)	0 (0)
Close contacts					
Yes	12 573 (18.57)	112 (11.43)	1382 (12.68)	7430 (18.31)	3649 (23.94)
No	44 749 (66.09)	741 (75.61)	8052 (73.89)	27 810 (68.52)	8146 (53.45)
Missing value	10 384 (15.34)	127 (12.96)	1463 (13.43)	5348 (13.18)	3446 (22.61)
Clustered cases					
Yes	6872 (10.15)	79 (8.06)	1016 (9.32)	4154 (10.23)	1623 (10.65)
No	38 834 (57.36)	586 (59.8)	6596 (60.53)	24 005 (59.14)	7647 (50.17)
Unknown	11 625 (17.17)	188 (19.18)	1829 (16.78)	7083 (17.45)	2525 (16.57)
Missing value	10 375 (15.32)	127 (12.96)	1456 (13.36)	5346 (13.17)	3446 (22.61)
Hubei Province*					
Wuhan	49 912 (73.72)	914 (93.27)	7922 (72.7)	28 508 (70.24)	12 568 (82.46)
Adjacent Wuhan districts	11 824 (17.46)	43 (4.39)	2074 (19.03)	7870 (19.39)	1837 (12.05)

Continued

Table 2 Continued

	Total (n (%))	Before 10 January (n (%))	10–22 January (n (%))	23 January–6 February (n (%))	7 February–7 March (n (%))
Non-adjacent Wuhan districts	5970 (8.82)	23 (2.35)	901 (8.27)	4210 (10.37)	836 (5.49)
Per capita GDP†					
Wuhan	49 912 (73.72)	914 (93.27)	7922 (72.7)	28 508 (70.24)	12 568 (82.46)
High	7051 (10.41)	26 (2.65)	1200 (11.01)	4758 (11.72)	1067 (7)
Low	10 743 (15.87)	40 (4.08)	1775 (16.29)	7322 (18.04)	1606 (10.54)
Migration rate‡					
Wuhan	49 912 (73.72)	914 (93.27)	7922 (72.7)	28 508 (70.24)	12 568 (82.46)
High	13 352 (19.72)	50 (5.1)	2302 (21.13)	8988 (22.14)	2012 (13.2)
Low	4442 (6.56)	16 (1.63)	673 (6.18)	3092 (7.62)	661 (4.34)
Travel intensity§					
Wuhan	49 912 (73.72)	914 (93.27)	7922 (72.7)	28 508 (70.24)	12 568 (82.46)
High	6305 (9.31)	22 (2.24)	1040 (9.54)	4300 (10.59)	943 (6.19)
Low	11 489 (16.97)	44 (4.49)	1935 (17.76)	7780 (19.17)	1730 (11.35)

*Adjacent Wuhan districts including Huangshi, Jingzhou, Ezhou, Huanggang, Xiaogan, Xianning and Xiantao, the rest were included in non-adjacent Wuhan districts.
†High per capita GDP districts of Hubei Province except for Wuhan including Yichang, Ezhou, Qianjiang, Xiangyang, Xiantao, Huangshi, Jingmen, Xianning, the rest were included in low group.
‡The migration rate is the mean of data from 1 to 23 January 2020. High migration rate districts of Hubei Province except for Wuhan, including Xiaogan, Huanggang, Jingzhou, Xianning, Ezhou, Xiangyang, Huangshi, Jingmen, the rest were included in low group.
§Travel intensity is the mean of data between 1 January 2020 and the date of blocking traffic connections. High travel intensity before the date of cordon sanitaire around the district except for Wuhan, including Xianning, Enshi Tujia and Miao, Huangshi, Yichang, Jingmen Tianmen, Shiyan, Xiangyang, the rest were included in low group.
GDP, gross domestic product.

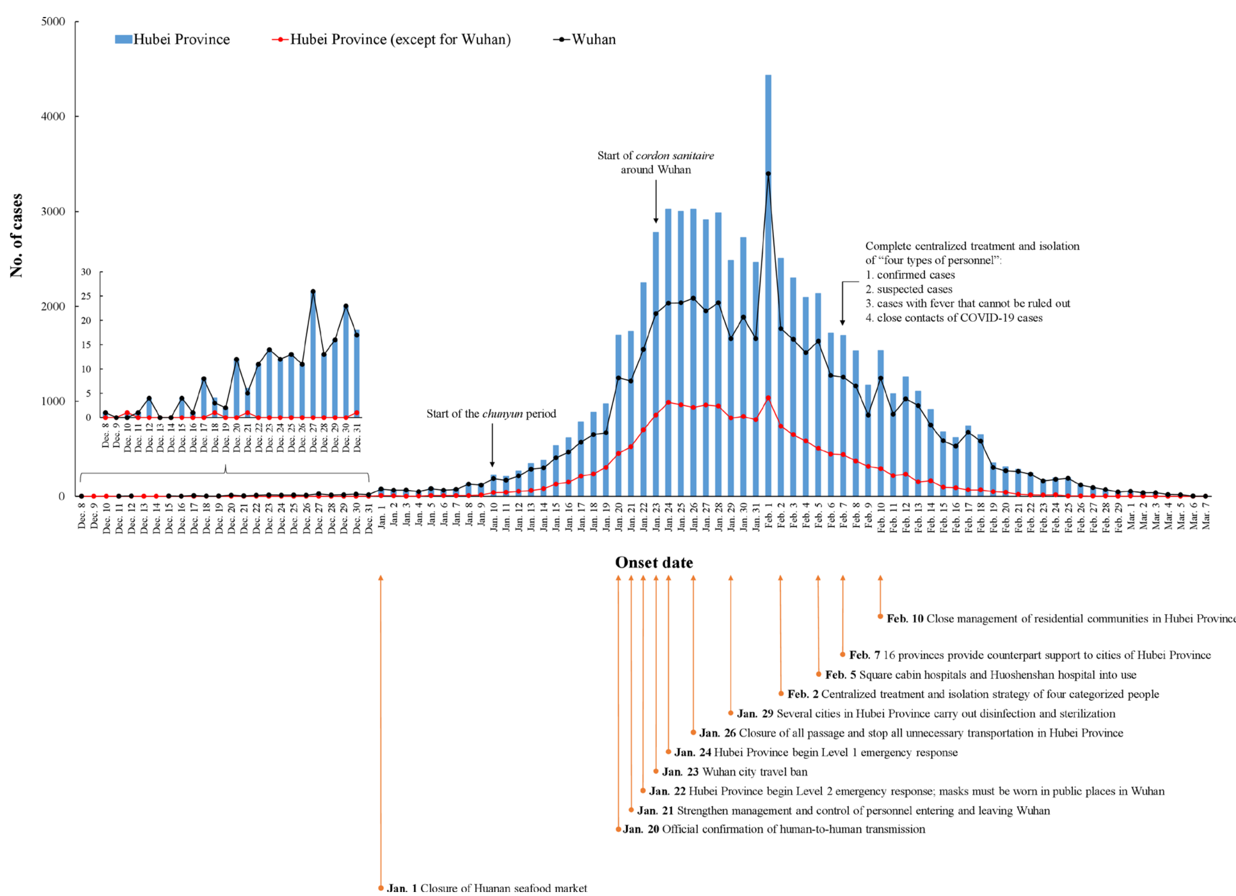

Figure 1 The daily COVID-19 onset and the important intervention measures in Hubei Province.

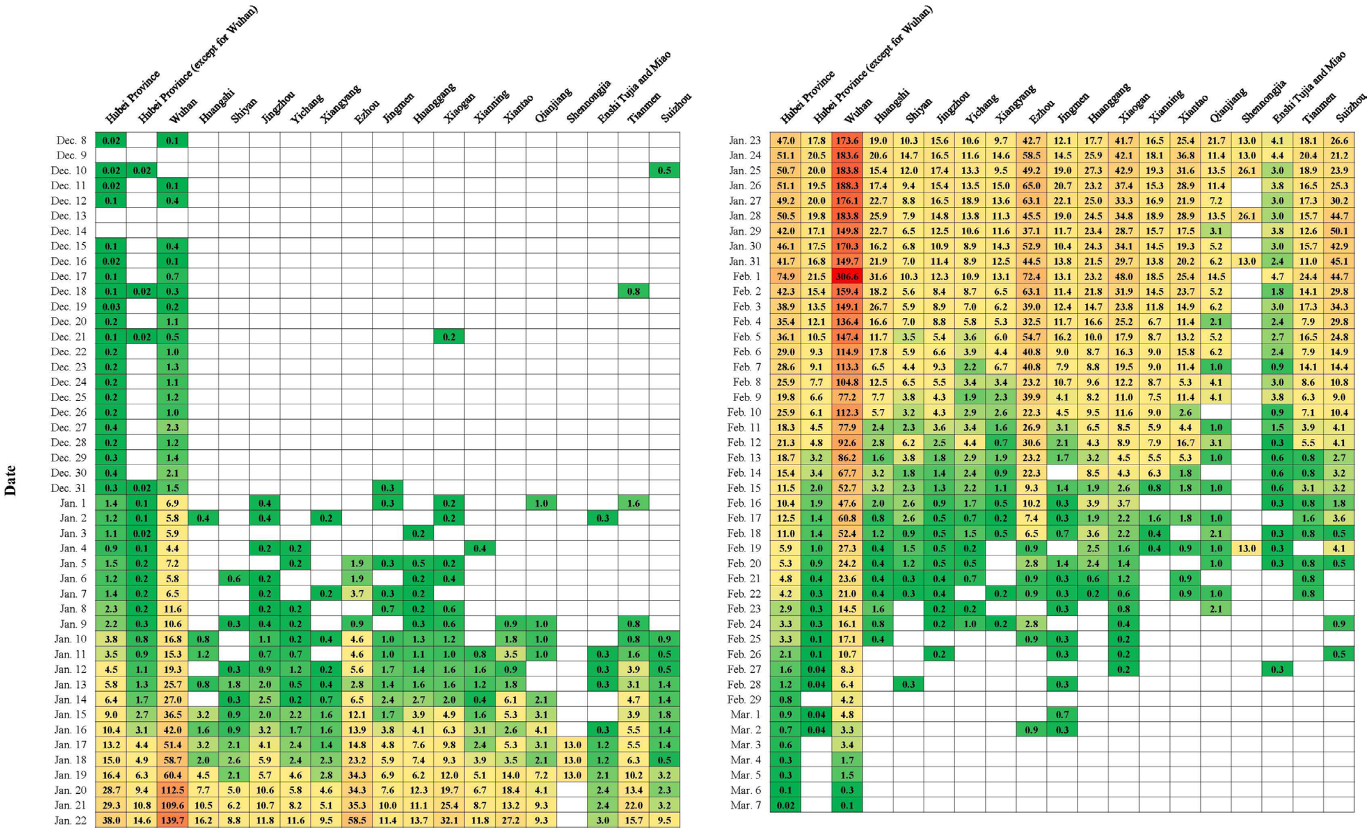

Figure 2 The daily onset situation and attack rates (per 106 people) of COVID-19 of 17 districts in Hubei Province.

9.3), for Hubei Province (except for Wuhan) were 0.04 (0.0 to 0.1), 4.8 (4.1 to 5.4), 16.7 (15.6 to 17.9) and 1.9 (1.5 to 2.2), and for Wuhan were 2.5 (2.2 to 2.8), 55.0 (53.6 to 56.4), 171.5 (169.1 to 174.0) and 37.8 (36.7 to 39.0), respectively. The daily average new cases and attack rates (/10^6) of COVID-9 in Wuhan were significantly higher than those in Hubei Province (except for Wuhan) in the same period (all $p<0.05$) (online supplemental table S1). Fourteen days (6 February) after 23 January, we observed a 33.8% decrease in daily attack rate (/10^6) in Wuhan, while a 48.0% decrease in Hubei Province (except for Wuhan); 14 days (21 February) after 7 February, the former was observed a 79.1% decrease and the latter was observed a 95.2% decrease (figure 2).

The global spatial autocorrelation analysis showed that the attack rates in Hubei Province were the scope of positive spatial agglomeration in the third period (online supplemental table S2). Local spatial autocorrelation results showed that Xiaogan and Ezhou were the high–high gathering, while Shennongjia and Yichang were the low–low gathering during the whole study period (all $p<0.05$). In the first study period, no local spatial autocorrelations were observed in Ezhou, Wuhan and Yichang (all $p>0.05$). However, in the last three periods,

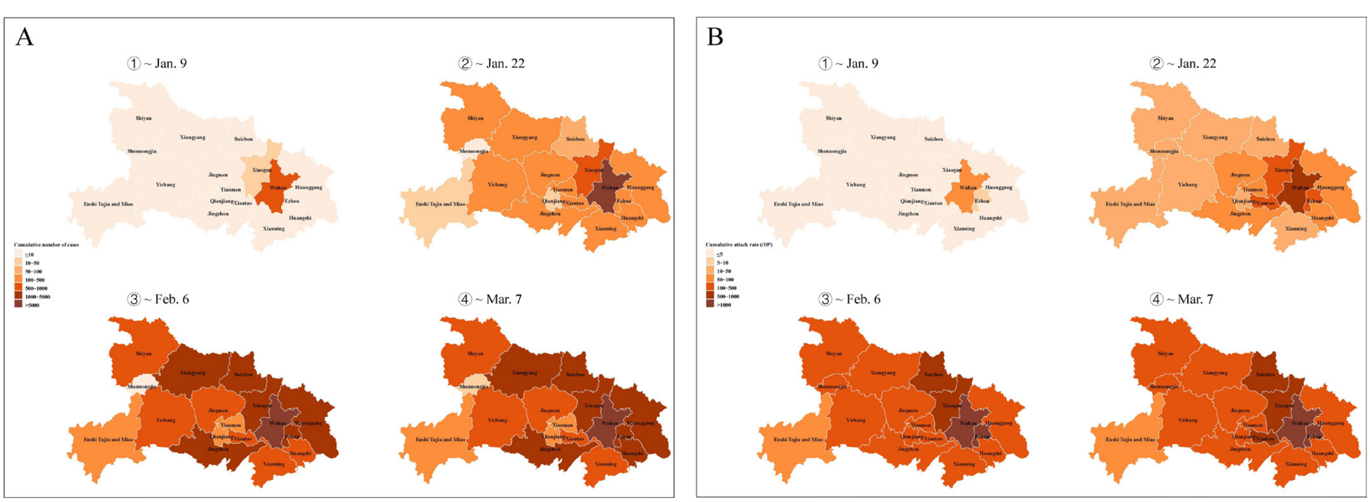

Figure 3 The spatiotemporal distribution of the cumulative number of cases and attack rate (per 106 people) of COVID-19 at four time points (9 January, 22 January, 6 February and 7 March 2020). (A) The cumulative number of cases; (B) the cumulative attack rates (per 10^6 people).

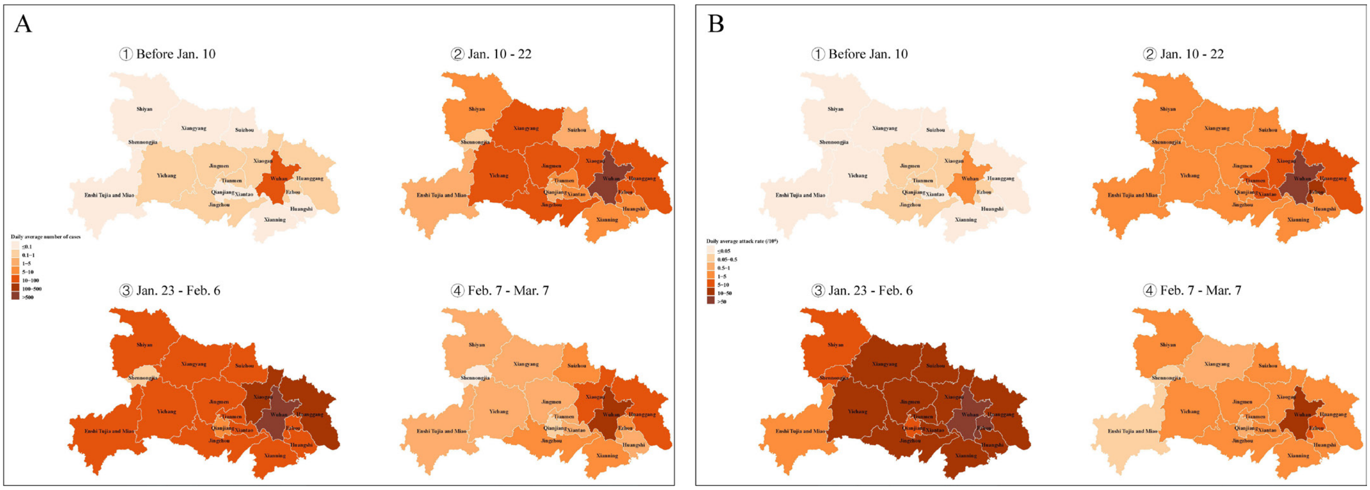

Figure 4 The daily average number of cases and attack rate (per 10^6 people) of COVID-9 during the four periods (before 10 January, 10–22 January, 23 January–6 February and 7 February–7 March). (A) The daily average number of cases; (B) the daily average attack rates (per 10^6 people).

high–high gathering, high–low gathering and low–low gathering were found in Ezhou, Wuhan and Yichang, respectively (online supplemental figure S1).

The doubling times of the total COVID-19 cases for Hubei Province, Hubei Province (except for Wuhan) and Wuhan in four periods is shown in online supplemental table S3. The harmonic means (95% CI) of doubling times in four periods for Hubei Province were 4.28 (4.01 to 4.55), 3.87 (3.78 to 3.98), 5.40 (4.83 to 6.05) and 45.56 (39.70 to 52.80) days and for Wuhan were 4.29 (3.96 to 4.56), 4.27 (4.16 to 4.42), 5.68 (5.12 to 6.34) and 40.80 (35.90 to 47.10), respectively. The harmonic means (95% CI) of doubling times in the last three periods for Hubei Province (except for Wuhan) were 2.34 (2.27 to 2.40), 4.77 (4.18 to 5.52) and 65.29 (54.80 to 79.9) days, respectively. Fourteen days (6 February) after 23 January, the doubling times of Wuhan and Hubei Province (except for Wuhan) increased by 95.0% and 133.2%, respectively. Fourteen days (21 February) after 7 February, the doubling times increased by 79.2% and 152.0%, respectively.

The changes in migration rate and travel intensity are shown in online supplemental figure S2. The travel intensity in each district increased slightly from the first period to the second period. After 23 January, all districts experienced a rapid decline to a low level, which continued to the end (online supplemental figure S2A). The two cities with the highest migration rates were Xiaogan and Huanggang, which increased obviously during the latter two periods (online supplemental figure S2B).

The epidemic curve based on both the onset date and diagnosis date of all cases is shown in online supplemental figure S3, and the median duration from onset to diagnosis in the above four periods is presented in figure 5. The median days from illness to diagnosis of Hubei Province in the first periods, the early stage of the outbreak, was 34 days. It then declined to 17 days in the second period and further to 9 and 4 days in the third and fourth periods, respectively.

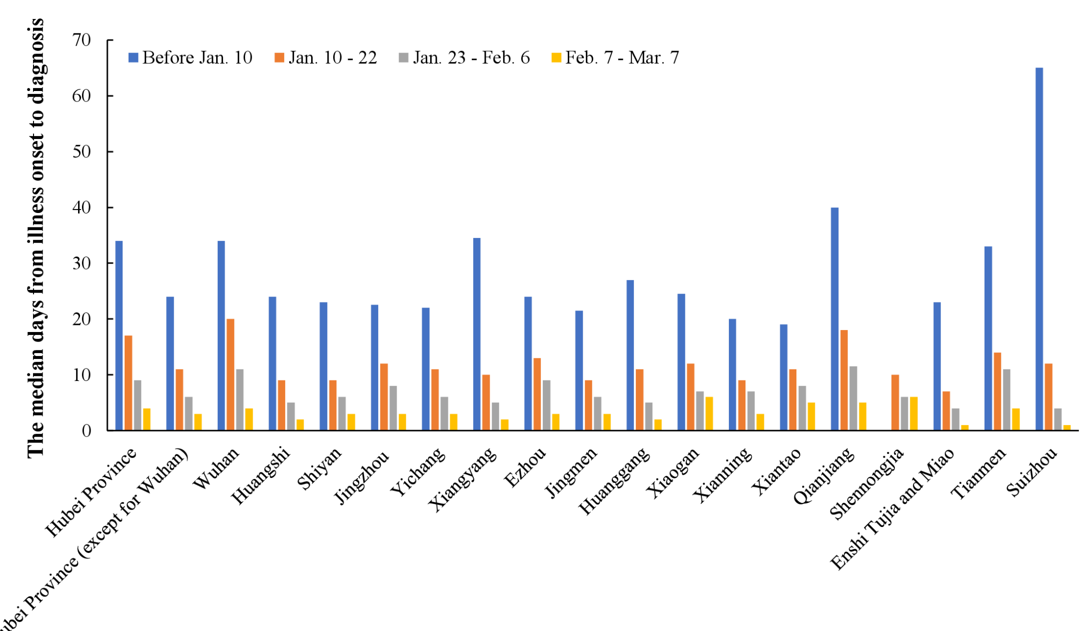

Figure 5 Median of time differences between illness onset and confirmed diagnosis of COVID-19 of 17 districts in Hubei Province during the four periods (before 10 January, 11–22 January, 23 January–6 February and 7 February–7 March).

DISCUSSION

The present study describes the population distribution and epidemic process of 67 706 COVID-19 cases in Hubei Province. By comparing the number of daily cases, attack rates, spatial clustering, doubling time and duration between onset and diagnosis in the four epidemic periods, we analysed the effects of non-pharmaceutical intervention measures, including district traffic interruption, wearing masks in public places and isolating infected patients and close contacts, on stopping the epidemic in Wuhan and Hubei Province (except for Wuhan) and found that the effects of these preventive measures were timely and obvious.

COVID-19 cases were heavily skewed towards the middle age and elderly, with a notable deficit of children. In the present study, 76.97% of patients were between 30 and 69 years old. The infection age distribution may be due to age-related differences in susceptibility to infection, behaviour or social activities.[11 17 18] We observed slightly more women (51.22%) than men (48.78%), which was inconsistent with early related reports.[8 19] According to the sex distribution of cases in this study, the proportion of males (50.20%) was higher than that of females (49.80%) in the first period, but the proportion of females (51.24%) was higher than that of males (48.76%) in the second to fourth periods. This may be related to more males being engaged in work or activities and having more opportunities to have contact with more people, including those infected. As the disease progresses and infection between family members occurs, the number of male and female cases tends to balance.[11] In the current study, more than 80% of COVID-19 cases were mild or common, and most COVID-19 cases did not know they were infected by SARS-CoV-2 until they had symptoms, which may be the main reason for the high transmission levels and lack of detection in the early stage.

We found that districts with high migration rates and districts adjacent to Wuhan resulted in more COVID-19 cases; however, districts with high travel intensity showed the opposite. This phenomenon indicated that the main risk factors for the spread of COVID-19 in non-epidemic areas may be large population movement and a close distance to the epicentre. In particular, after the traffic interruption of Wuhan on 23 January, the number of daily new cases in the neighbouring districts showed a one-way downward trend. Of course, it is necessary to isolate cases in time and require all residents to stay at home in these districts.

We classified the entire outbreak into four periods according to three important time points that may affect the spread of COVID-19. In the first period (before 10 January), a total of 980 cases were reported in Hubei Province, among which more than 90% were in Wuhan. In the second period (10–22 January), we observed a rapidly increasing number of daily attack rate (/10^6) both in Wuhan and in other districts in Hubei Province, from 16.8 and 0.8 on 10 January to 139.7 and 14.6 on 22 January, respectively. However, we found that the harmonic mean (95% CI) of doubling times in Hubei Province (except for Wuhan) (2.34 (2.27 to 2.40) days) was faster than that in Wuhan (4.27 (4.16 to 4.42) days) during this period. A possible reason may be that a large number of floating populations poured out of Wuhan to other districts in Hubei Province due to the start of the Spring Festival travel rush, accelerating the increase in COVID-19 cases.[11] On 20 January, officials confirmed human-to-human transmission of COVID-19, and 3 days later, decisive measures were taken to contain the spread of the epidemic. In the third period, high levels of daily attack rate were observed in and outside Wuhan until 2 February. The main reason is that the export of cases from Wuhan decreased in other districts but that the cases in Wuhan district were not well isolated, even though the government required the residents to stay at home and wear masks in public places. Also, some people who were infected with SARS-COV-2 before 23 January developed COVID-19 after an average incubation period of 5–6 days.[20] Our results show that the growth rate of doubling times in Hubei Province (except for Wuhan) was faster than that in Wuhan during the third period, which indicates that the impact of the Wuhan travel ban was more profound in other districts. The government adopted centralised treatment and isolation of 'four types of personnel' to further curb the spread of the epidemic on 2 February, which had been completed basically in Hubei Province by 7 February. In the last period (7 February–7 March), the daily attack rate (/10^6) of Wuhan and other districts in Hubei Province further decreased greatly, from 113.3 and 9.1 on 7 February to 0.1 and 0 on 7 March, and the doubling times increased significantly (from 23.39 and 29.42 days on 8 February to 78.21 and 149.83 days on 7 March). If we use the average attack rate for the third period (45.7 per 10^6) to calculate the total number of infected cases in the fourth period, we find that intervention measures could reduce the number of 65 935 cases (44 448 in Wuhan and 21 487 in other districts in Hubei Province). In brief, our study shows that all intervention measures were confirmed to be greatly effective in stopping the spread of COVID-19.

In the present study, due to the lack of diagnostic reagents and insufficient awareness of emerging infectious diseases, the interval between the onset of disease symptoms and the time of diagnosis was long before 10 January, which cause patients or asymptomatic cases to spread the disease at an early stage. After 10 January, the level of medical care continued to improve, especially the tremendous investment in healthcare resources, which greatly shortened the time from onset to diagnosis, from 34 days in the first period to 4 days in the fourth period. Take the diagnostic reagents for example, the daily sample detection capacity in Hubei Province was about 200 copies before 19 January, but this number increased to about 4000 by 29 January and 10 000 by 5 February.[21 22] Sufficient nucleic acid detection reagents have been provided since 12 February 2020; the detection ability in Hubei Province was further improved.[13] The shortening of the time between symptom onset and diagnosis speeds up the detection and isolation of cases, effectively reduced the chance of exposure and spread of COVID-19.[18]

This study has several limitations. First, we lack sufficient investigation to describe each case's exposure to the source of infection because so many cases appeared and there were not enough public health doctors. Second, clinically diagnosed cases were included in the analysis. However, clinically diagnosed cases, such as laboratory-confirmed cases, have similar epidemiological histories, clinical symptoms and, most importantly, similar CT imaging findings, which provide a guarantee for the diagnosis of cases in outbreaks when diagnosed reagents are lacking. Also, a clinical diagnosis needs to be confirmed by multiple clinicians. Follow-up studies should further refine the prevalence, evolution, clinical manifestations, laboratory examination and imaging detection of cases, providing a solid foundation for the prevention and treatment of COVID-19. Third, due to the lack of diagnostic reagents for laboratory detection, the number of COVID-19 and asymptomatic cases was underestimated in the early stage, for example, before 19 January. A city-wide screen study in Wuhan in the postlockdown phase of 14 May to 1 June 2020, showed that 300 asymptomatic positive cases of 9 899 828 participants with a detection rate of 0.303

(95% CI 0.270 to 0.339)/10 000 were found in Wuhan city.[23] According to this rate, about 455 (95% CI 406 to 510) asymptomatic cases were missed in Hubei Province, which may deviate our epidemiological picture slightly. Of course, due to the good effects of the isolation measures, the number of new cases was 0 in April in Hubei province, and the proportion of asymptomatic infections may be lower than that in early January 2020.

We observed the outbreak process of COVID-19 in Hubei Province from 8 December 2019 to 7 March 2020, with 56 days from the first case to the peak point. The number of new daily cases and attack rate decreased significantly after the closure of Wuhan, and the isolation of four types of personnel effectively controlled increased numbers of cases. At the same time, our study shows that the median time from onset to diagnosis after the adoption of the above-mentioned control measures was also significantly reduced, which effectively decreased the number of cases and added strength to the successful control of the epidemic.

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