The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China

Short title: COVID-19 and lockdown

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Abstract

Background:

With its epicenter in Wuhan, China, the COVID-19 outbreak was declared a public health emergency of international concern (PHEIC) by the World Health Organization (WHO). Consequently, many countries have implemented flight restrictions to China. China itself has imposed a lockdown of the population of Wuhan as well as the entire Hubei province. However, whether these two enormous measures have led to significant changes in the spread of COVID-19 cases remains unclear.

Methods:

We analyzed available data on the development of confirmed domestic and international COVID-19 cases before and after lockdown measures. We evaluated the correlation of domestic air traffic to the number of confirmed COVID-19 cases and determined the growth curves of COVID-19 cases within China before and after lockdown as well as after changes in COVID-19 diagnostic criteria.

Results:

Our findings indicate a significant increase in doubling time from 2 days (95% Confidence Interval, CI): 1.9-2.6), to 4 days (95% CI: 3.5-4.3), after imposing lockdown. A further increase is detected after changing diagnostic and testing methodology to 19.3 (95% CI: 15.1-26.3), respectively. Moreover, the correlation between domestic air traffic and COVID-19 spread became weaker following lockdown (before lockdown: $r=0.98$, $p<0.05$ vs. after lockdown: $r=0.91$, $p=NS$).

Conclusions:

A significantly decreased growth rate and increased doubling time of cases was observed, which is most likely due to Chinese lockdown measures. A more stringent confinement of people in high risk areas seem to have a potential to slow down the spread of COVID-19.

1. Introduction

The current outbreak of coronavirus (COVID-19) in Wuhan and the entire Hubei province has caused global concerns. With continuously rising numbers of confirmed cases, a COVID-19 pandemic is becoming a reality. Current detailed knowledge on the biology and transmission of this virus is limited[1,2], and COVID-19's final mortality rates are subject to rough estimation. According to some sources, the estimated date of first COVID-19 cases has been reported around January 2nd, 2020 while other data indicate cases starting on December[3,4]. On December 31st, 2019 pneumonia of unknown origin is first reported by the World Health Organization (WHO).

Consequently, international flight traffic has been greatly affected, and Hubei province was placed under lockdown approximately 3 weeks after the start of COVID-19 outbreak. In Wuhan, the imposed lockdown resulted in travel restrictions to and from Wuhan to ensure rigorous adherence to home quarantine. Social distancing was practiced by canceling events and gatherings, closing of public places as well as schools and universities. Additionally, outside activities were extremely limited since every citizen was given a permission card and only allowed to leave their home every second day for a maximum of 30 minutes. Despite this rigorous enforcement launched by China to contain COVID-19 spread, total case numbers have significantly increased in China as well as internationally. These developments transform the current COVID-19 outbreak into a global pandemic.

Interestingly, there are different measures to contain COVID-19 infections and reduce interaction between unidentified infected and non-infected individuals. In a recent study, Wilder-Smith et al.[5] describe these different concepts in detail, ranging from quarantine of confirmed and possibly infected individuals as implemented in Germany to community containment in northern Italy with travel restriction outside of defined areas, and point out their respective efficacy in virus containment. We know from previous studies that travel restrictions have demonstrated a positive effect in past SARS, Ebola and bubonic plague outbreaks[6 – 8]. The measures implemented in Wuhan and the entire Hubei region of China exceed by far the classic definition of local confinement, lockdown and isolation.

Lockdown is now increasingly implemented in Europe, with the entire nation of Italy in lockdown. However, as opposed to the rigorous measures implemented in Hubei, Italian authorities have allowed residents to continue working, as well as eating out until 6pm if they respect a 1m distance to other guests. However, lockdown measures and confinement raise serious concerns in the population, as they are distant memory of a tainted European past, dating back to sieges of cities in the middle ages and bubonic plague outbreaks. Before COVID-19, the most recent and tragic occasion of population confinement in Europe was the establishment of Jewish ghettos in Warsaw and other cities during German Nazi rule.

Concerns have been voiced that, at this stage, COVID-19 spread can no longer be retained in many countries. The aim of this study is to evaluate whether rigorous lockdown measures as implemented by China have the potential to slow down the virus' spread. In this current environment, it is crucial to understand and assess the total effect of these combined measures and policies, as their efficacy remains unclear. For further clarification, the most relevant statistical terms have been described below:

Doubling time: time for a given quantity to double in size or number at a constant growth rate
Serial interval: time between successive cases in a chain of transmission
R0: basic reproductive number indicating disease transmission. R0 reflects the average number of secondary infections produced by a typical infection case in a population where everyone is susceptible

2. Materials & Methods

Acquiring exact data on Chinese air traffic is challenging. Currently, the Civil Aviation Administration of China (CAAC) has partially restricted access to information on passenger volume, destinations and locations. At the same time, only a few studies have focused on the domestic and international connection of the Chinese aviation market[9,10]. Restricted access to current data therefore requires analysis of available data and studies on the Chinese aviation market and other countries.

Timeline: lockdown period and changes in COVID-19 diagnostic criteria

The onset of COVID-19 was estimated to be in December[4]. Wuhan City and the major cities in Hubei, China were put under lockdown on the 23rd and 24th of January, respectively. Thus, we defined the lockdown period as going into effect from the 23rd to 25th of January. On February 7th, China announced changes in diagnostic criteria to confirm COVID-19 cases.

Data sources

China Domestic Air Traffic and Passenger Throughput

According to the CAAC, China is divided into 4 economic regions: East China, Northeast China, Central China and West China. The domestic passenger throughput data from 2018 for each economic region were sourced from the publicly available annual civil aviation industry report from CAAC. CAAC databases did not include domestic air traffic in 2019; therefore, air traffic in 2019 within China was not included in the analysis.

Confirmed Cases of COVID-19

The total number of confirmed COVID-19 cases for each region in China and reported outside of China were sourced from the COVID-19 situation reports made publicly available by the WHO. The present study included data from January 20th, 2020, which was the first COVID-19 situation report published by WHO, until February 13rd, 2020 (figure 1).

Distribution of confirmed COVID-19 cases with unspecified regions in China on January 23rd, 2020

On January 23rd, 2020, WHO reported 131 confirmed cases of COVID-19 with unspecified regions in China. As domestic air traffic in China has been used to forecast the spread of COVID-19 outbreak, we first distributed these cases to each economic region in China based on the ratio of passenger throughput in each economic region to the total number of passenger throughput in China in 2018 (East China: 70 cases, Northeast China: 8 cases, Central China: 15 cases, West China: 38 cases)[3]. We further distributed these cases to each province according to the ratio of the population in each province to the total population in each economic region of China in 2018. The data for the population in each province and economic region of China was sourced from the annual database made publicly available by the National Bureau of Statistics of China (figure 2).

Outcome measures and statistical analysis

Changes of cases before and after quarantine (figure 2)

We presented the total numbers of COVID-19 cases for the Hubei province. Then, we calculated the medium amount of cases reported in each Chinese economic region. Those medium numbers were based on total case numbers per province in each region that had reported COVID-19 cases. Based on these numbers we derived a standard mean of the error for each region. For the Central region, Hubei province, which is the epicenter of the outbreak, was not included. Data is presented in Figure 2. All continuous measurements are presented as mean ± standard error of the mean. A one-way ANOVA followed by a post-hoc Tukey's HSD test was performed to determine the statistical significance in the number of confirmed COVID-19 cases in each Chinese economic region before and after the start of the lockdown period until the introduction of changes in COVID-19 diagnostic criteria.

Correlation of passenger throughput and COVID-19 cases before and after lockdown (figure 3)

Historical flight patterns demonstrated by passenger throughput predict the expected distribution pattern of COVID-19 spread in China, radiating from the epicenter in Wuhan[11]. Since case numbers in Wuhan are assumed to be extremely high, distribution patterns should be linked to this epicenter as long as case numbers in Wuhan are overwhelming. This has already been confirmed in figure 1. Therefore, a correlation between the air traffic and the distribution of COVID-19 was calculated using the least square regression line. The total numbers concerning the passenger throughput in percent for each economic region was (37.2×10^7 West, 67.3×10^7 East, 7.9×10^7 Northeast and 14×10^7 Central.) The passenger throughput for each region and the corresponding COVID-19 cases were demonstrated before (figure 3 A) and 13 days after (figure 3 B) lockdown. The two different timepoints used were 1) before the lockdown period on January 24th, 2020 and 2) after the lockdown period on February 7th, 2020. Analysis included calculation of r, r^2 and p-values. Cases in Hubei province were not included in the cases of the Central province. Correlation analysis was evaluated using linear regression to determine growth curves. P-values <0.05 were considered statistically significant. GraphPad Prism (GraphPad Software 8.0.1) was used for all analyses.

Growth of COVID-19 cases at different time intervals

We determined growth curves of total case number in China at three distinct timepoints:

1) before the lockdown period of Hubei province (January 20th, 2020 - January 25th, 2020)

2) during lockdown in Hubei province (January 26th, 2020 - February 27th, 2020)

3) onset of changes in diagnostic criteria

An exponential growth curve was approximated according to these time intervals $\boldsymbol{C_{1\text{-}3}}$:

C_1 x :[20-25.January] $x \longmapsto$ [1-5]
C_2 x :[26.January-7.February] $x \longmapsto$ [1-13]
C_3 x :[8.February-27.February] $x \longmapsto$ [1-20]

C(x) represents calculated COVID-19 cases in total numbers at each time point **x** based on the current cases $\mathbf{C_k}$ and the doubling time **d** in days. The approximated doubling time of cases is described by **d** for each time interval

$$C_{1,2,3}(x) = C_k \cdot 2^{\frac{x-1}{d_{1,2,3}}}$$

A descriptive figure of the approximated curves for each distinct interval is presented in figure 4. In figure 5, all distinct time intervals are presented with extension of the curves assuming no interventions e.g. lockdown or changes in diagnostic criteria had occurred. Exponential growth analysis was used to determine growth curves (extension of intervals). GraphPad Prism (GraphPad Software 8.0.1) was used for all analyses

Development of cases with direct travel history to China
Outside of China, we quantified the number of new confirmed COVID-19 cases from January 20th, 2020 to February 13th, 2020. These cases where then separated into 2 groups according to recent travel history to China. Cases where lined up on a timeline and correlation analysis was evaluated using linear regression. Exponential growth analysis was used to determine growth curves. P-values <0.05 were considered statistically significant. GraphPad Prism (GraphPad Software 8.0.1) was used for all analyses.

3. Results

Confirmed COVID-19 cases before and after the start of the lockdown period
Distribution analysis of confirmed COVID-19 cases before and after the start of the lockdown period showed significant differences. The average case numbers per province within Central China and Hubei massively increased from 5.5 ± 1.5 and 375 to 594 ± 252 and 22112, growing approximately 5900% and 10800%, respectively (p<0.01, figure 2). However, the numbers in peripheral regions grew slower from 9 ± 2.6, 4.2 ± 1, and 2 ± 0.3 cases before lockdown to 380.10 ± 90, 136 ± 41, and 121 ± 53 cases after lockdown in eastern, western, and northeastern China, respectively (p<0.01, p=NS, p=NS, respectively, figure 2). Following the lockdown period, case numbers in eastern China were significantly higher than in western China (p<0.05, figure 2). Similarly, case numbers in central China were significantly higher than in western and northeastern China after lockdown (p<0.05, p<0.05, figure 2).

Correlation of confirmed COVID-19 cases to domestic passenger throughput in each economic region of China before and after the start of the lockdown period. Analysis of confirmed COVID-19 cases in Chinese economic regions showed a significant correlation with 2018 domestic passenger throughput before the lockdown was in effect ($r=0.98$, $r^2=0.97$, $p<.05$, figure 3A). This correlation became weaker following the lockdown period ($r=0.91$, $r^2=0.83$, p=NS, figure 3B). With the lockdown in effect, case distribution loses its correlation to the disease epicenter.

Growth curve analysis of confirmed COVID-19 cases prior to the lockdown period, following the lockdown period, and after changes in COVID-19 diagnostic criteria

A continuous decrease in growth was observed. This was corresponding to the increased doubling time of COVID-19 cases. Before the lockdown period this number was approximately 2 days (1.9, 95% CI:1.4-2.6). After the lockdown period it was 4 days (3.9, 95% CI:3.5-4.3). However, doubling time changed massively after the start of new definitions and diagnostic criteria after February 7th. At this last interval the doubling time was 19 days (19.3, 95% CI:15.1-26.3). However, both the reported data and the corresponding curve in this third interval become relatively erratic and diagnostic criteria change multiple times.

Distribution of confirmed COVID-19 cases outside of China

Analysis of confirmed COVID-19 cases outside of China showed a shift from cases with travel history to China to cases with either confirmed or possible transmission outside of China. The first group with travel history to China seemed to have already peaked as of February 13th, 2020. However, cases without travel history to China do not follow this path (figure 6).

4. Discussion

While a further COVID-19 spread could not be contained, the measures attributed to the lockdown in Hubei aided in slowing the speed of infection and reducing the correlation of domestic air traffic with COVID-19 cases within China. When interpreting the observed changes in doubling time all measures imposed in Wuhan must be considered. Our data cannot differentiate which of the stringent measures were most successful, as our analyses only assessed the efficacy of the totality of these measures. The totality of these measures was partially successful and have resulted in a delayed COVID-19 spread in China. Currently, international cases have already outnumbered reported cases in China; therefore, containment of a global COVID-19 spread seems unfeasible. Although a doubling time of 19 days is overserved in the latest interval, the reasons behind this observation remain difficult to discern.

It is possible that, to a large extent, this observation is explained by multiple changes in COVID-19 diagnostic criteria. While measurable effects were achieved by the described lockdown efforts in the Hubei province, more attention should be directed toward the new epicenters outside of China in order to slow down COVID-19 spread. As Wilder-Smith et al. have already pointed out, early measurements are needed to contain or at least significantly slow down the virus' spread. Yet, due to political and economic considerations, the degree of transparency in reporting and efforts in detecting COVID-19 cases as well as the willingness to implement

countermeasures drastically varies from country to country. A basic reproductive number (R_0) had been estimated based on different models ranging from 2.2-3.9[12,13]. However, these numbers only make sense in their respective context and it is recommended not to compare values based on different models.
R_0 numbers show variations as they depend on multiple factors, including number of susceptible individuals exposed to infected COVID-19 patients. A recently conducted, very small-scale study on COVID-19 estimated a serial interval of 4-5 days, therefore suggesting that a substantial proportion of secondary transmission may occur prior to illness onset[14].

The overall international development of COVID-19 cases remains concerning and a further large trend of underreporting must be assumed. This is a negative development and indicates that COVID-19 will become a pandemic, especially considering that countries such as Iran, South Korea, Japan and Italy have reported large numbers of cases. If China cannot contain COVID-19 cases within its borders despite enormous efforts, the question will arise as to whether other countries can.

It is most likely going forward that despite continuing restrictions in air traffic, shipping, or other means of transportation, COVID-19 will eventually spread and create global virus pockets with possible new mutated strains of the virus. While the current focus is shifting from China to the new epicenters and their lockdown, new information on the virus are available nearly daily, a development which may raise knowledge and awareness on how to contain COVID-19.

5. Conclusion

Our data indicate a significant decrease in the growth rate. Moreover, we observe a corresponding increase in the doubling time of COVID-19 cases within China, which can be possibly attributed to rigorous Chinese lockdown measurements. However, as the number of cases outside of lockdown areas have increased, there are significant concerns for a pandemic. The COVID-19 outbreak continues across China and new epicenters are developing across the globe. Stringent containment measures should be considered for heavily affected regions to buy time and enable medical facilities to cope with increasing intensive care cases.

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Author contribution:

HL: data acquisition, data interpretation, final analysis, drafting of the manuscript, final approval for publication
VK: data acquisition, analysis and interpretation, drafting of the manuscript, final approval for publication
PK: data interpretation, drafting of the manuscript, final approval for publication
AM: data interpretation, drafting of the manuscript, final approval for publication

JS: data interpretation, drafting of the manuscript, final approval for publication
JB: data interpretation, critical revision for important intellectual content, final approval for publication
TK: data interpretation, conception and design of the work, critical revision for important intellectual content, final approval for publication

Conflict of interest:
The authors declare that they have no conflicts of interest.

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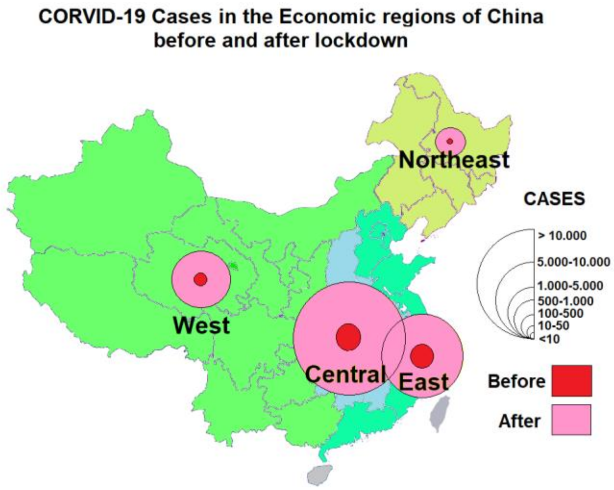

Figure 1: Total number of COVID-19 cases in Chinese economic regions before and after lockdown. Case numbers according to WHO data.

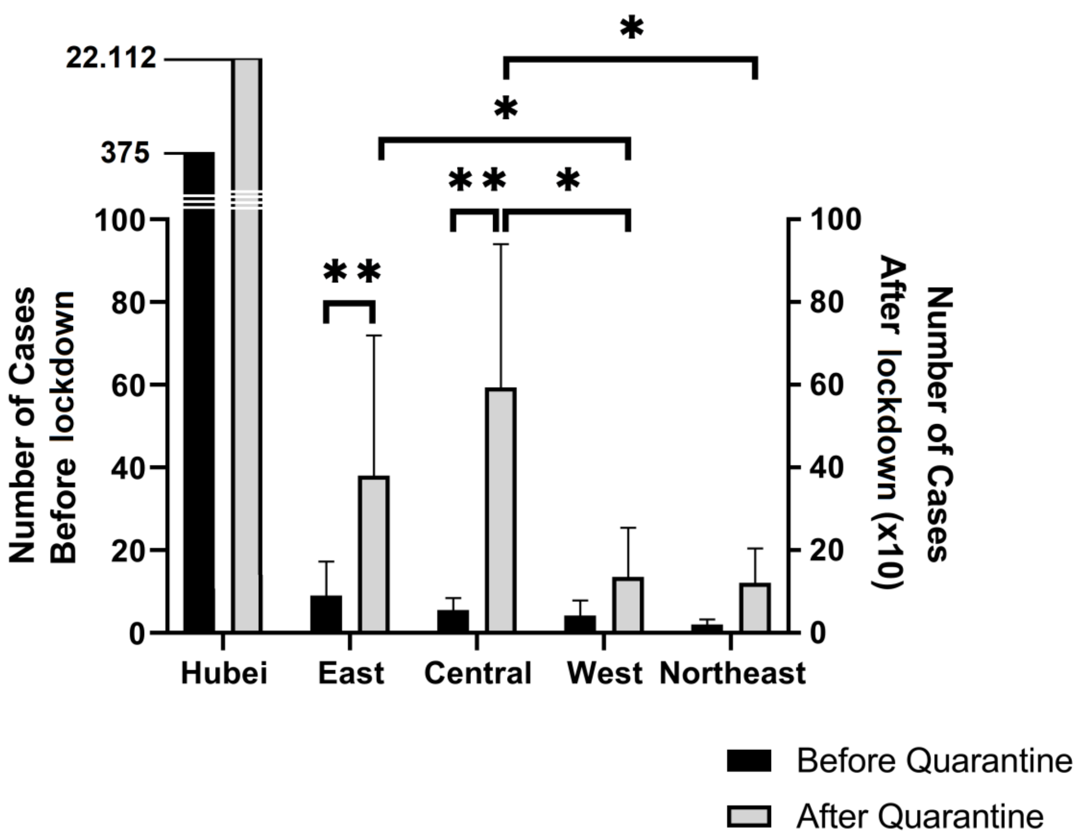

Figure 2: Mean number of COVID-19 cases of in the economic regions for each province before and after lockdown. Hubei province was excluded from the central province and separately examined. Based on these numbers we derived a standard mean of the error for each region.

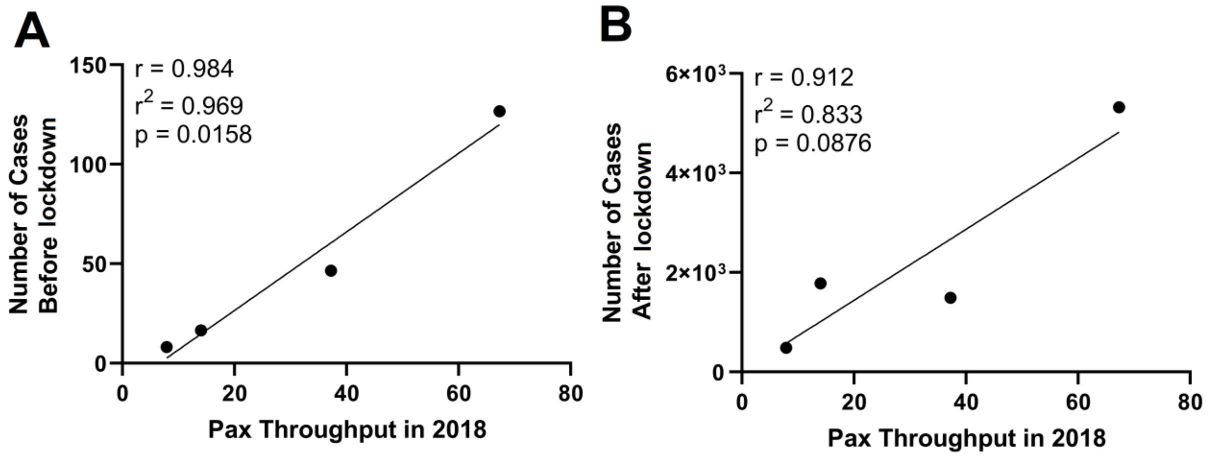

Figure 3: Correlation between passenger throughput as an indicator for air-traffic intensity and COVID-19 cases before (A) and after lockdown (B) for Chinese economic regions

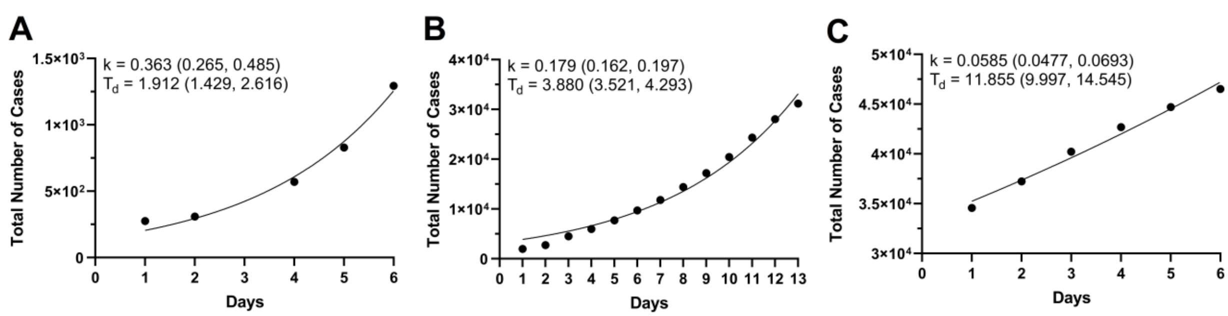

Figure 4: Development of COVID-19 cases in China before (A) and after lockdown (B) until February 7th. (C) cases after February 7th when multiple changes in diagnostic criteria were announced. Approximation of the growth curves to each interval

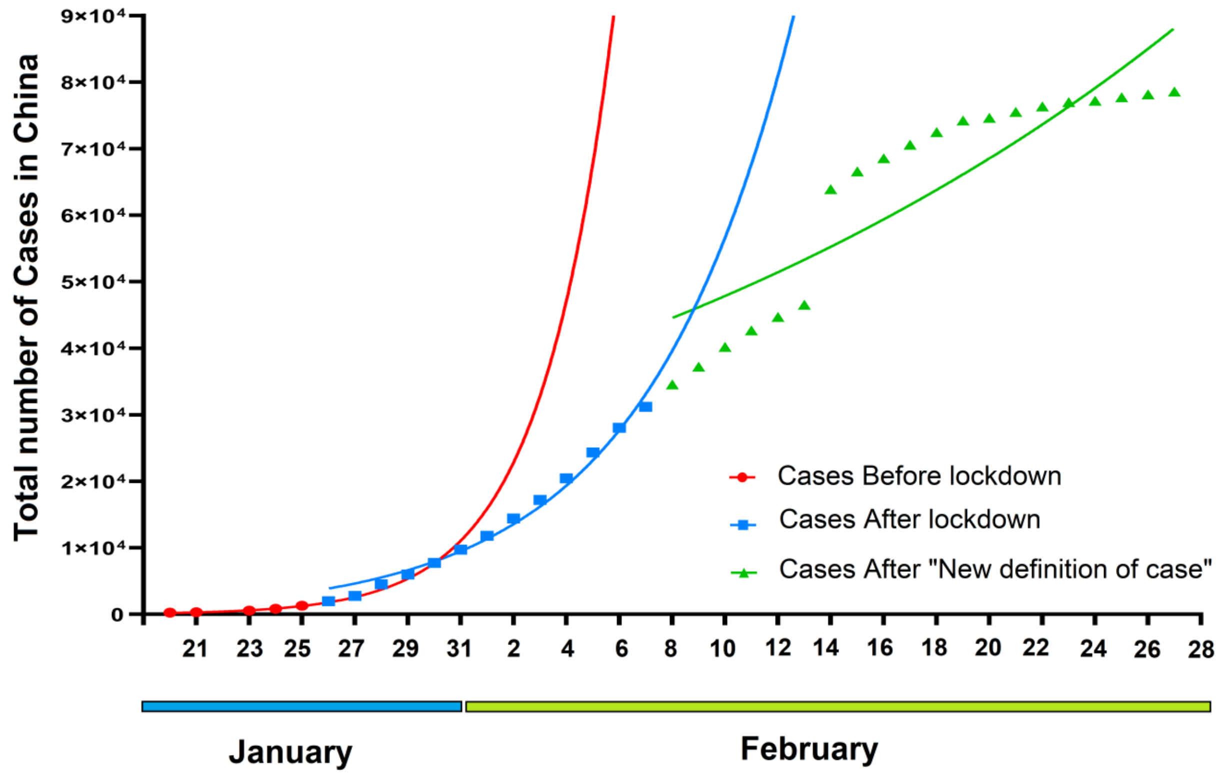

Figure 5: Extension of growth curves for three distinct time intervals (cases before lockdown, cases after lockdown and cases after new diagnostic criteria)

1. Red dots: first reported COVID-19 cases before lockdown measures were implemented
2.Red line: potential number of COVID-19 cases if lockdown measures had not been implemented; calculations are based on approximated doubling
3. Blue dots: reported COVID-19 cases after lockdown measures
4. Blue line: potential number of COVID-19 cases if no changes had been made in diagnostic criteria; calculations are based on approximated doubling
5. Green dots: reported COVID-19 cases after implemented changes in diagnostics
6. Green line: approximated growth curve for COVID-19 cases under new diagnostic criteria

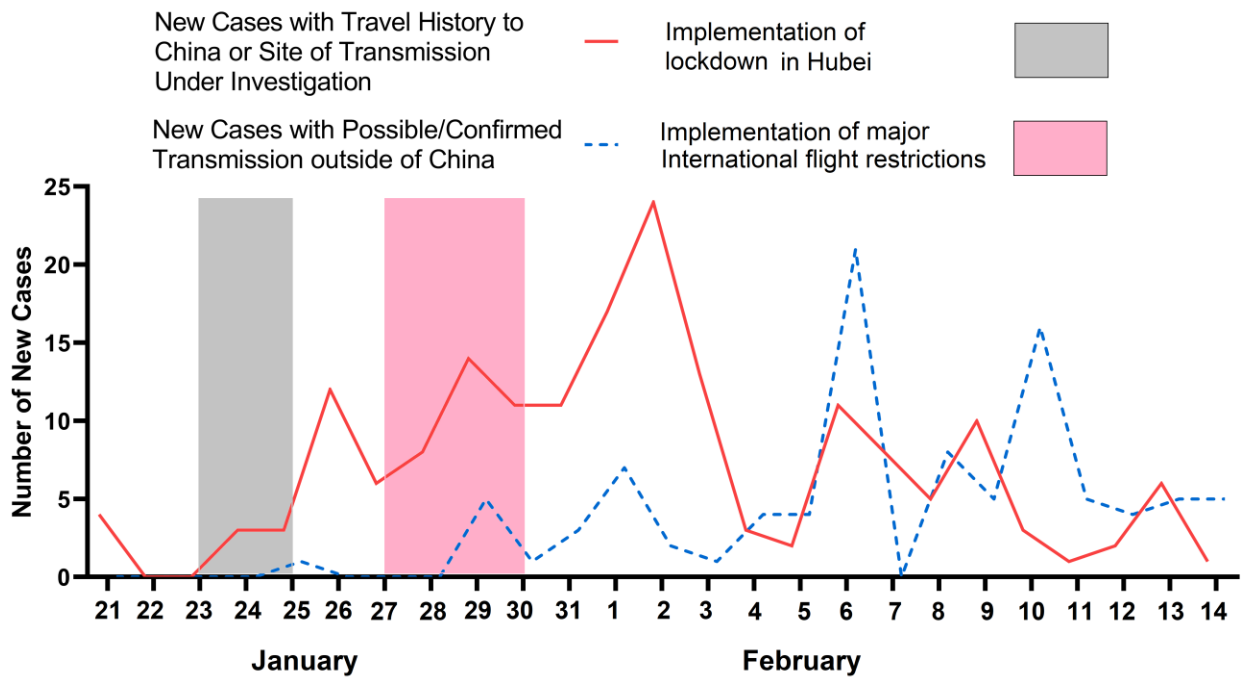

Figure 6: Confirmation of new international COVID-19 cases with and without travel history to China in relation to implemented measures (lockdown and flight restrictions)