International Journal of Infectious Diseases 97 (2020) 1–6

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Estimating the instant case fatality rate of COVID-19 in China

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ARTICLE INFO

Article history:
Received 31 March 2020
Received in revised form 19 April 2020
Accepted 21 April 2020

Keywords:
COVID-19
Case fatality rate
Cure rate
China

ABSTRACT

Objective: The outbreak of coronavirus disease 2019 (COVID-19) in China has been basically controlled. However, the global epidemic of COVID-19 is worsening. We established a method to estimate the instant case fatality rate (CFR) and cure rate of COVID-19 in China.
Methods: A total of 82 735 confirmed cases released officially by the Chinese authorities from December 8, 2019 to April 18, 2020 were collected. The estimated diagnosis dates of deaths and cured cases were calculated based on the median cure time or median death time of individual cases. Following this, the instant CFR was calculated according to the number of deaths and cured cases on the same estimated diagnosis date.
Results: In China, the instant CFR of COVID-19 was 3.8–14.6% from January 1 to January 17; it then declined gradually and stabilized at 5.7% in April. The average CFR in China was 6.1 ± 2.9%, while the CFR was 1.0 ± 0.4% in China except Hubei Province. The cure rate of COVID-19 was 93.9 ± 2.9% in China, and stabilized at 94.3%, while it was 99.0 ± 0.4% in China except Hubei Province.
Conclusions: The instant CFR of COVID-19 in China overall was much higher than that in China except Hubei Province. The CFR of COVID-19 in China was underestimated.

1. Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is of great concern. As of April 19, 2020, the number of confirmed COVID-19 cases had passed 2 160 000 worldwide (World Health Organization, 2020a). More than 82 000 cases had been confirmed and more than 4600 patients had died in China. At present, the outbreak in China has been essentially controlled. More than 100 countries worldwide are now facing and dealing with the COVID-19 epidemic, including the United States, Spain, Italy, Germany, Iran, France, the United Kingdom, and South Korea.

For an unprecedented epidemic such as COVID-19, it is important to assess its hazards. The case fatality rate (CFR) is the ratio of the number of deaths divided by the number of confirmed cases over a certain period of time. This is the most direct index to reflect the lethality of the disease. Since the occurrence of the epidemic in China, the CFRs of COVID-19 have been examined in many studies published in the literature. However, the literature on CFRs of COVID-19 is subject to several limitations. When a pandemic is still ongoing, the resulting CFR (the number of deaths divided by the number of confirmed cases), called the naive CFR, does not represent the true CFR (Kucharski and Edmunds, 2014).

One reason for this is that the rate ignores patients who are still hospitalized. The outbreak is not over, so the numbers of confirmed cases, cured cases, and deaths are still subject to change. Hospitalized patients will either recover or die in the future. Among the published studies, Huang et al. reported that 41 confirmed patients had been discharged, six patients had died (15%), and the remaining seven patients were still hospitalized (Huang et al., 2020). Wang et al. reported that 47 of 138 confirmed cases were discharged, six died (4.3%), and the remaining 85 patients were still hospitalized in Wuhan, China (Wang et al., 2020a,b). Zhang performed an analysis of the characteristics of 72 314 patients reported in the Chinese Infectious Disease Information System (Zhang, 2020). Among the 44 672 confirmed

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https://doi.org/10.1016/j.ijid.2020.04.055

cases, a total of 1023 deaths occurred, with a CFR of 2.3%. However, there were still 38 909 hospitalized cases among the 44 672 confirmed cases. There is a large discrepancy in the COVID-19 CFRs reported in the current literature and in official announcements (Battegay et al., 2020). Therefore, it is unreasonable to integrate all hospitalized patients into the denominator to calculate the case fatality. Another reason is that the death dates are later than the diagnosis dates during the period of the outbreak, which could increase the error of the estimation of the CFR.

These two reasons will lead to an underestimation of the CFRs of COVID-19 when the epidemic is still ongoing. China was the first country affected and the first to recover in the outbreak. An incorrect estimation of the CFR of COVID-19 may have a considerable impact on global epidemic prevention, and make the global pandemic worse.

The World Health Organization (WHO) has called on every country to act with speed, scale, and clear-minded determination. Estimating and predicting the CFR are very important to assess the hazards of COVID-19 regarding epidemiology. This might provide the basis for the formulation of public security strategies, the allocation of health resources, and the adjustment of medical treatment work. It might also be helpful to government decision-making and improving public understanding.

This study was performed to establish a method to estimate the instant CFR of COVID-19 in China, including and excluding Hubei Province. The method was expected to avoid the interferences of hospitalized cases and the delay in cure dates or death dates. The estimation of a more accurate fatality rate for COVID-19 has a significant role in providing a basis for the prevention and control of this infectious disease.

2. Materials and methods

2.1. Data sources and collection

The accumulated data of COVID-19 cases in China from December 8, 2019 to April 18, 2020 were collected from the websites of the National Health Commissions of the People's Republic of China (http://www.nhc.gov.cn/xcs/xxgzbd/gzbd_index.shtml), Health Commissions of Hubei Province (http://wjw.hubei.gov.cn/fbjd/dtyw), and Health Commissions of Wuhan City (http://wjw.wh.gov.cn/front/web/list3rd/yes/802). One hundred and forty-one individual death cases and 580 individual cured cases were also collected, for which detailed treatment history including information about diagnosis date, discharge date, and death date were available.

2.2. Research design and data analysis

The CFR is defined as the percentage of deaths in the total number of confirmed cases of COVID-19. After treatment, the confirmed patients had two endpoints, either cure or death, which would occur on dates later than their confirmed cure time and death time. In order to estimate the CFR, first the cure time and death time, and then the confirmed dates of cured cases and deaths should be calculated.

The data consisted of the number of newly confirmed cases (N_i), the number of newly cured cases (C_i), the number of new deaths (D_i), the number of cumulative confirmed cases (CD_i), the number of cumulative cured cases (CC_i), and the number of cumulative deaths (Cd_i) per day (i).

Cure time (T_C) was the period from diagnosis date (D_D) to discharge date (D_S). Death time (T_D) was the period from D_D to death date (D_d).

$$T_C = D_S - D_D$$

$$T_D = D_d - D_D$$

The T_C of 580 cured cases and T_D of 141 individual deaths were analyzed to obtain the mean cure time (MT_C) and mean death time (MT_D). Based on MT_C or MT_D, the diagnosis dates of cure cases and deaths were estimated, respectively. It was assumed that the cured patients experienced MT_C after diagnosis. The estimated diagnosis date (D_{eD}) of cured patients should be the date on MT_C, before the announced cure date.

$$D_{eD} \text{ of cured cases} = D_S - MT_C$$

It was assumed that the patients who died experienced a period of M_D after diagnosis. The estimated diagnosis date (D_{eD}) of death should be the date on MT_D, before the announced death date (Fig. 1).

$$D_{eD} \text{ of death} = D_d - MT_D$$

The number of cumulative cured cases on D_{eD} was set as CC_{ei}. The number of cumulative deaths on D_{eD} was set as Cd_{ei}. On the same estimated diagnosis date (D_{eD}), the number of cumulative confirmed cases (CD_{ei}) was equal to the sum of the number of cumulative cured cases (CC_{ei}) and the number of cumulative deaths (Cd_{ei}).

$$CD_{ei} = CC_{ei} + Cd_{ei}$$

The daily CFR (CFR_i) was equal to the number of cumulative deaths (Cd_{ei}) divided by the number of cumulative confirmed cases

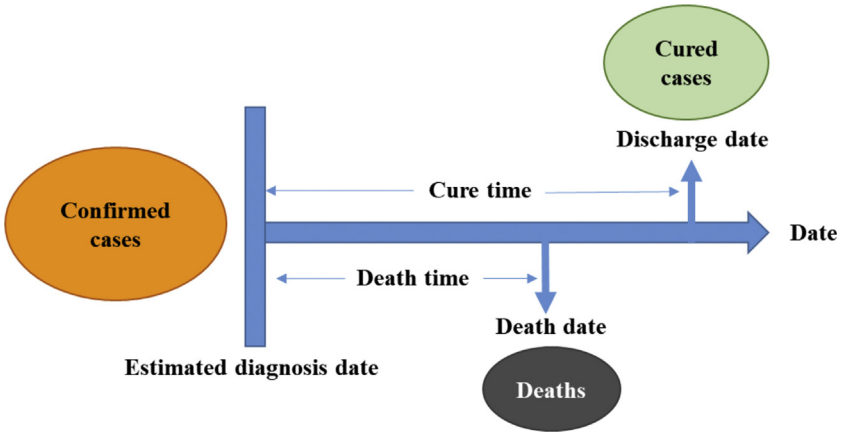

Fig. 1. Relationship of the estimated diagnosis date and date of case notification for deaths and cured cases.

(CD_{ei}) on the same estimated diagnosis date.

$$CFR_i = Cd_{ei}/CD_{ei} \times 100\%$$

The daily cure rate (CR_i) was equal to the number of cumulative cured cases (CC_{ei}) divided by the number of cumulative confirmed cases (CD_{ei}) on the same estimated diagnosis date.

$$CR_i = CC_{ei}/CD_{ei} \times 100\%$$

2.3. Statistical analysis

Excel 2016 and GraphPad Prism 8 were used to record the data, perform calculations, analyze the data, and draw the graphs. The unit of time for the data collection of epidemic disease cases was 1 day. A Gaussian distribution was used to analyze the characteristics of the cure time and death time obtained from 580 cured cases and 141 individual deaths.

3. Results

3.1. Daily newly confirmed cases of COVID-19

Fig. 2 shows the curves of daily newly confirmed cases of COVID-19 reported in China and in China except Hubei Province. The initial confirmed cases appeared on December 8, 2019, in China and on January 19, 2020, in China except Hubei Province. The number of daily newly confirmed cases in China increased from early January 2020, peaked in the first half of February, and then gradually fell (Fig. 2A). The percentage of daily newly confirmed cases in China except Hubei Province and in China was over 50% from January 18 to January 26 and then sustained a downward trend. After January, the daily numbers of newly confirmed cases in China except Hubei Province were much lower than those in China. The number of daily newly confirmed cases was less than 30 in the middle of March, but showed a tendency to grow from the end of March to April. The number of daily newly confirmed cases was less than 30 from April 16 to April 18. Moreover, the increased cases were mainly from China except Hubei Province.

The cured cases in China initially occurred on January 3, 2020, continued to increase in the second half of January and the first half of February, and achieved a peak at the end of February. In China except Hubei Province, the number of cured cases was less than that in China, and its peak appeared in mid-February, gradually decreasing to the end of March, and showing a tendency to increase in April (Fig. 2B).

In China, the deaths began to increase from mid-January to late January in 2020, with a peak at 254 cases on February 12, then gradually decreasing to less than 10 from mid-March to mid-April. The death toll in China except Hubei Province showed no obvious change and was within the range of 0–8 cases per day from late January to April (Fig. 2C).

The average numbers of daily newly confirmed cases, daily newly cured cases, and daily new deaths in China except Hubei Province were 109 cases, 101 cases, and 1 case, respectively, which were far lower than those in China at 630, 731, and 32 cases, respectively.

3.2. Cumulative cases of COVID-19

The daily cumulative cases of COVID-19 curves are shown in Fig. 3. Up to April 18, 2020, there were 82 735 confirmed cases, 77 062 cured cases, and 4632 deaths in China, and only approximately 18% of confirmed cases ($n = 4632$), 18% of cured cases ($n = 13\,555$), and 2.6% of deaths ($n = 120$ deaths) were in China except Hubei Province. The cumulative confirmed cases and the cumulative cured cases followed an 's' curve increase. The increase in cumulative confirmed cases began in early January, accelerated

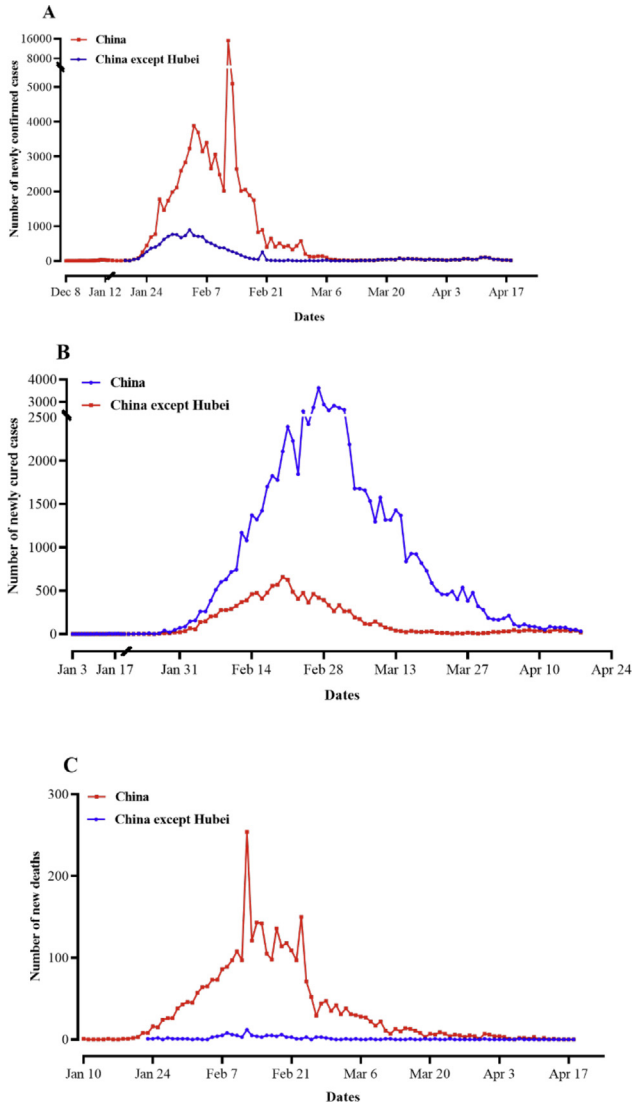

Fig. 2. Daily new cases of COVID-19 in China and in China except Hubei Province: (A) daily newly confirmed cases; (B) daily newly cured cases; (C) daily new deaths.

from mid-January to February, and stabilized in March. The increase in cumulative cured cases began in mid-January, accelerated from February to early March, and gradually stabilized at the end of March. The increase in the cumulative death toll began in mid-January, accelerated in early February, slowed down in late February, and stabilized from March to April.

In China except Hubei Province, the increases in cumulative confirmed, cured, and death cases occurred later and were lower than those in China. On April 17, the government taskforce of Wuhan charged with virus prevention added 325 confirmed cases and 1290 deaths, and reduced the number of cured cases in the city by 965, taking the confirmed count to 3869 from a previously reported 2579, the death count to 50 333 from 50 008, and the cured count to 46 335 from 47 300 up to April 16, 2020.

3.3. Death time and cure time

According to the diagnosis dates and death dates of 141 death cases, the death time from diagnosis to death was calculated. The mean death time, median death time, and quartile spacing of COVID-19 were 9.75 ± 7.2 days, 8 days, and 11 days, respectively. The cure time from diagnosis dates to discharge dates was also

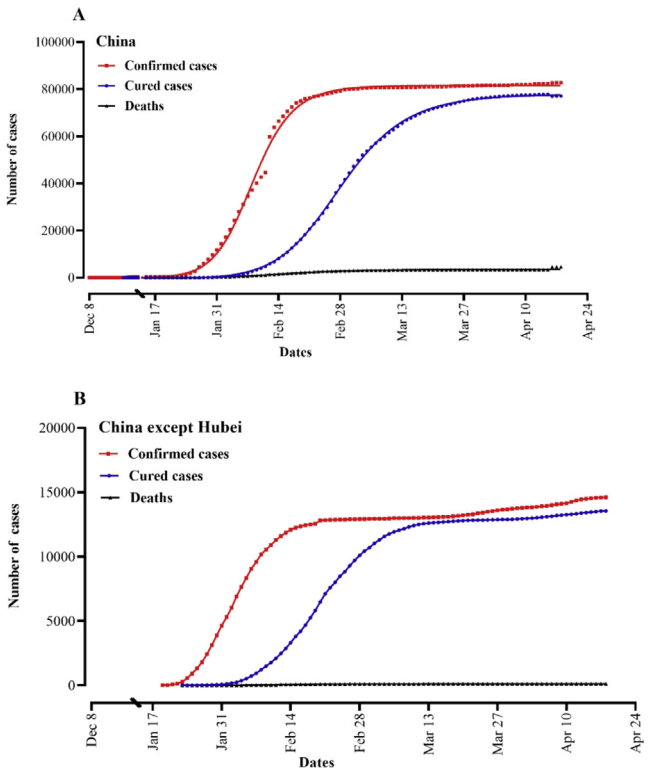

Fig. 3. Daily variation curve of cumulative cases of COVID-19 (A) in China, and (B) in China except Hubei Province.

calculated based on the diagnosis dates and discharge dates of 580 cured cases with COVID-19. The curve of cure time for COVID-19 patients displayed a left skewed distribution with a skewness of 1.09 ± 0.10. The mean cure time was 14.6 ± 6.7 days with a 95% confidence interval of 6.9–21.0 days, and the median cure time was 13 days. Based on the proportion of cumulative confirmed cases that were cured, it was estimated that the median cure time of COVID-19 in the country was 15 days.

3.4. Diagnosis dates of deaths and cured cases

Based on the median death time of 8 days obtained from individual deaths, the D_{eD} of deaths was estimated, which was equal to the death date reported on daily case notification data minus 8 days. Based on the results of the median cure time of 15 days, the D_{eD} of cured cases was estimated to be the discharge date on daily case notification data minus 15 days. The curves of the numbers of cumulative deaths, cumulative cured cases, and the sum of cumulative deaths and cumulative cured cases of COVID-19 on the estimated diagnosis dates in China and in China except Hubei Province are shown in Fig. 4.

3.5. Case fatality rates of COVID-19

Depending on the estimated diagnosis dates on the same day of deaths and cured cases, the instant CFR and cure rate of COVID-19 in China and in China except Hubei Province were calculated; these are shown in Fig. 5. In China, the instant CFR of COVID-19 ranged from 3.8% to 14.6%. The CFR was less than 10% (3.8–9.1%) from January 1 to January 13, 2020, increased continuously to 14.6% on January 17, and then gradually declined and stabilized at 4.2% on April 7, which is an estimated diagnosis date. However, based on the corrected data reported by the government taskforce of Wuhan on April 17, the CFR was increased to 5.7% from the previously estimated 4.2%. The average CFR in China was $6.1 \pm 2.9\%$. The CFR of COVID-19 in China except Hubei Province was 0.5% to 3.4% in the early stage from February 15 to March 25. Thereafter, the CFR tended to be stable and less than 1%. The average CFR in China except Hubei Province was $1.0 \pm 0.4\%$. The CFR of COVID-19 in China except Hubei Province was markedly lower than that in China as a whole.

3.6. Cure rates of COVID-19

The instant cure rate of COVID-19 in China was high at 95% in early January, gradually declined to 85.5% in the middle of January, and then slowly increased and stabilized at nearly 95.9% on April 7, which is an estimated diagnosis date (Fig. 5A). However, based on the corrected data reported by the government taskforce of Wuhan, the cure rate was decreased to 94.3% from the previously estimated 95.9%. The average instant cure rate of COVID-19 in China was $93.9 \pm 2.9\%$. The instant cure rate of COVID-19 in China except Hubei Province ranged from 96.6% to 98.9% in the early stage from February 15 to February 23, and then remained at the high level of 99.1%. The average cure rate reached $99.0 \pm 0.5\%$. The cure rate of COVID-19 in China except Hubei Province was clearly higher than that in China.

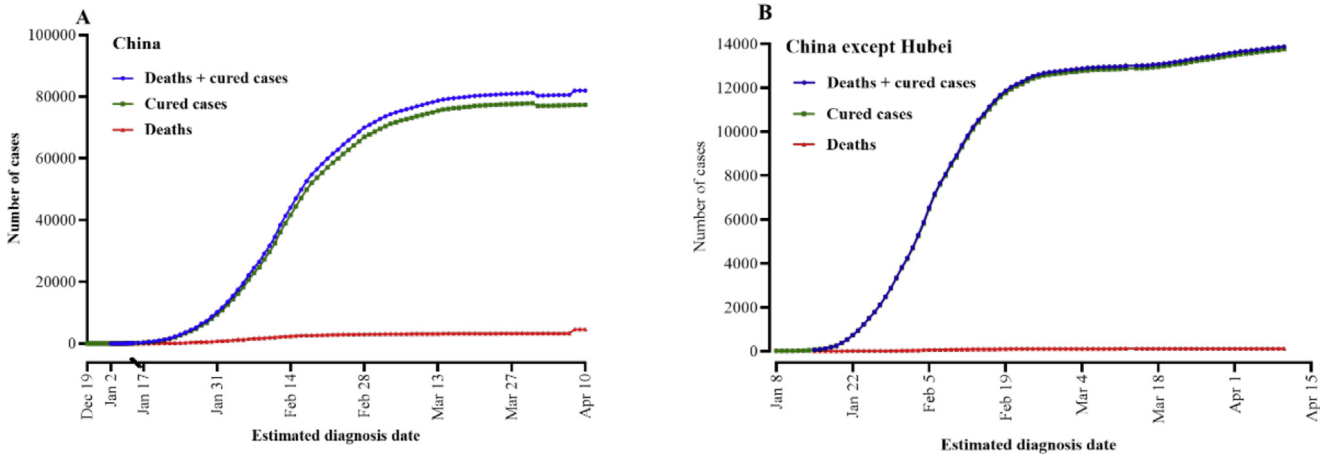

Fig. 4. Numbers of deaths and cured cases on the estimated diagnosis dates of COVID-19 in (A) China, and (B) China except Hubei Province.

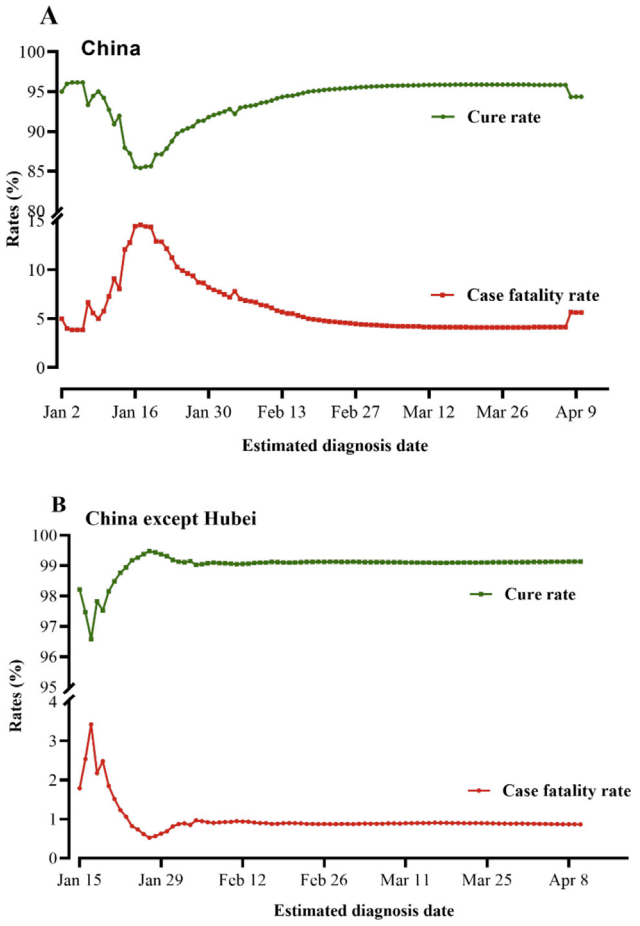

Fig. 5. Instant fatality rates and cure rates of COVID-19 in (A) China, and (B) China except Hubei Province.

3.7. Mortality rate of COVID-19

As of April 18, 2020, the numbers of deaths with COVID-19 was 4632 in China and 120 in China except Hubei Province. The population of China is 1.40 billion and of Hubei Province is 59.27 million. The mortality rates of COVID-19 were 0.33/100 000 in China and 0.009/100 000 in China except Hubei Province.

4. Discussion

The current outbreak of COVID-19 has become a pandemic and the global outbreak is getting worse. The assessment of hazards of the outbreak is important to its hazard assessment . However, the high proportion of hospitalized patients and the intervals between diagnosis dates and death dates or cure dates increased the deviation of the estimation of the CFR during the outbreak, especially in the early stage. Based on the average death time and average cure time, we estimated the endpoint (cure and death) of the confirmed cases on the estimated diagnosis date, and obtained the CFR and cure rate of COVID-19. This new method of estimation can avoid the interference of hospitalized cases and the delay of cure dates or death dates.

A total of 82 735 confirmed COVID-19 cases in China were collected. The majority of the confirmed cases (82%) in China were from Hubei Province. Hence, the characteristics of COVID-19 cases in China and in China except Hubei Province were analyzed. The number of daily newly confirmed cases in China increased from early January 2020. In order to block the route of transmission, the government of China announced traffic control and robust containment and control activities. The spread of the virus was slowed through the implementation of this blockade (World Health Organization, 2020b). In March, the outbreak had basically been controlled in China.

In brief, on February 17, the Director General of the WHO said that patients with COVID-19 have a “mild disease and will recover” and that it is fatal in 2% of reported cases. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team reported that the CFR of COVID-19 was approximately 2.3%, based on 1023 deaths among 44 672 confirmed cases. However, 54% of patients were still hospitalized, some of whom died in the future. The CFR of COVID-19 may be underestimated.

In this study, it was assumed that the cured patients or patients who died experienced a ‘cured time’ or ‘death time’ period after diagnosis. The estimated diagnosis dates of cure cases and deaths were approximated based on the median cure or death time obtained from individual cases. Using the numbers of deaths and cured cases on the same estimated diagnosis date to calculate the daily CFR avoided the interference of hospitalized cases and the time delay, thereby reflecting the actual situation of deaths. The instant CFR of COVID-19 in China increased continuously from 4% to 15% in mid-January 2020. Since then, the treatment concept and methods have been, the treatment level has improved, and the treatment procedure has become increasingly standardized . The CFR gradually declined and stabilized at 4.2%. However, based on the corrected data reported by the government taskforce of Wuhan on April 17, the CFR was increased to 5.7% from the previously estimated 4.2%. The average CFR in China was 6.1%. The CFR of COVID-19 in China except Hubei Province was 1%, which was lower than that in the country as a whole.

The cure rate and fatality rate are opposite competitive pairs. The average instant cure rate of COVID-19 in China was 93.9%. Depending on the characteristics of the change in the instant cure rate of COVID-19 in China, the instant cure rate tended to be stable at 95.9%. However, based on the corrected data reported by the government taskforce of Wuhan on April 17, the cure rate was decreased to 94.3% from the previously estimated 95.9%. The cure rate of COVID-19 in China except Hubei Province was approximately 99%.

This study has its limitations. The selection of cure time and death time could affect the reliability of the results. Increasing the number of individual deaths and cured cases could decrease the deviation from reality. In addition, we used the median time of deaths and cured cases. However, the death time and cure time may be different on different days.

In conclusion, we established a method to estimate the CFR and the cure rate of COVID-19. This method avoided the interferences of hospitalized cases and the delay of cure dates or death dates. In China, the CFR ranged from 3.8% to 14.6%, and stabilized at 5.7% in April. The average CFR in China was 6.1%. The cure rate was 94.3% in April. In China except Hubei Province, the CFR of COVID-19 was 1% and the cure rate was 99%.

Declarations

Funding sources: This study was supported by grants from the National Natural Science Foundation of China (No. 81803647and No. 81670001).

Ethical approval: Ethical approval was not required.

Conflict of interest: We declare no competing interests.

Author contributions

YXC and LC were responsible for the conceptual design and led the team. YNM, YXC, and LC drafted and revised the manuscript.

YNM, TTH, JXZ, QQ, YXG, SYL, HMX, and CHN were responsible for the data collection and management. All authors read the manuscript and contributed to editing.

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