

RESEARCH ARTICLE

The COVID-19 outbreak in Sichuan, China: Epidemiology and impact of interventions

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Abstract

In January 2020, a COVID-19 outbreak was detected in Sichuan Province of China. Six weeks later, the outbreak was successfully contained. The aim of this work is to characterize the epidemiology of the Sichuan outbreak and estimate the impact of interventions in limiting SARS-CoV-2 transmission. We analyzed patient records for all laboratory-confirmed cases reported in the province for the period of January 21 to March 16, 2020. To estimate the basic and daily reproduction numbers, we used a Bayesian framework. In addition, we estimated the number of cases averted by the implemented control strategies. The outbreak resulted in 539 confirmed cases, lasted less than two months, and no further local transmission was detected after February 27. The median age of local cases was 8 years older than that of imported cases. We estimated R_0 at 2.4 (95% CI: 1.6–3.7). The epidemic was self-sustained for about 3 weeks before going below the epidemic threshold 3 days after the declaration of a public health emergency by Sichuan authorities. Our findings indicate that, were the control measures be adopted four weeks later, the epidemic could have lasted 49 days longer (95% CI: 31–68 days), causing 9,216 more cases (95% CI: 1,317–25,545).

Author summary

Since its emergence in Wuhan, SARS-CoV-2 rapidly started its spread across China. On January 21, 2020 the first COVID-19 case was detected in the Sichuan Province of China and led to an outbreak of local transmission. Less than two months later, the outbreak was over with the last reported case on March 4, 2020. In this study, we analyzed patient records for all laboratory-confirmed cases reported in Sichuan to provide an epidemiological

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characterization of the outbreak, to estimate SARS-CoV-2 transmission potential, and to assess the impact of the adopted interventions. We estimated that, during the initial exponential growth phase of the outbreak, each COVID-19 case has generated a mean of 2.4 secondary cases (95% CI: 1.6–3.7). Moreover, we estimated that, were the Sichuan strict containment measures implemented four weeks later, the outbreak would have caused 9,216 more cases (95% CI: 1,317–25,545). Our findings suggest the key role of a quick response to COVID-19 outbreaks and the importance of an adequate surveillance and monitoring system.

Introduction

SARS-CoV-2 has been incredibly successful in spreading swiftly from Wuhan, Hubei Province in China. The number of cases rocketed and the disease spread through China, quickly entering an exponential growth phase [1]. Non-pharmaceutical interventions were quickly put in place both at the epicenter of the outbreak and country-wide, culminating in the implementation of the lockdown of entire populations with the goal to suppress or mitigate the epidemic to prevent overwhelming health care systems [2,3].

Chinese provinces outside Hubei represent an important example of successful local containment of COVID-19 outbreaks and thus represent a valuable source of information for other countries as well. Sichuan is one of the largest provinces of China with a population size of about 83-million individuals and a major transport hub in Southwestern China. Sichuan was one of the first provinces outside Hubei to record COVID-19 cases with a first importation from Wuhan detected on January 21, 2020 [4]. Then, despite the importations of several tens of cases from Wuhan/Hubei over a relatively short period of time (less than 2 months), a major epidemic wave was avoided. As of June 22, 2020, 589 cases are reported by the CDC of Sichuan province [5].

The aim of this study is to describe the epidemiological characteristics of the COVID-19 outbreak in the Sichuan and to shed light on its successful local containment. By using a Bayesian approach based on the renewal equation [6,7], we estimated the basic and daily reproduction numbers. The posterior distribution of the reproduction number has been used to project the number of cases in case the adopted interventions had started between one and four weeks later. This allowed us to estimate the number of averted cases, including severe and critical ones.

Materials and methods

Ethics statement

The study was approved by the Clinical Trials and Biomedical Ethics Committee of West China Hospital, Sichuan University (No. 2020190). Data were deidentified, and informed consent was waived.

Data

Case definition. All cases were PCR confirmed. The severity of cases (paucisymptomatic, symptomatic, severe, and critical) is classified according to the fifth version of “Guideline on diagnosis and treatment of novel coronavirus infected pneumonia (NICP)” issued by China CDC on February 4, 2020 [5]. Briefly, mild cases are defined as cases showing mild clinical symptoms and no radiographic evidence of pneumonia. Symptomatic cases present clinical symptoms, such as fever and respiratory symptoms as well as radiographic evidence of

pneumonia. Severe cases have to meet one of the following conditions: i) respiratory rate interval ≥ 30 b.p.m.; ii) SpO₂ (saturation of peripheral oxygen) $\leq 93\%$ at rest; iii) PaO₂/FiO₂ ≤ 300 mmHg (1mmHg = 0.133kPa). Critical cases have to meet one of the following conditions: i) respiratory failure and consequent needs of mechanical ventilation; ii) shock; iii) require intensive care because of multiple organ dysfunction.

Case data. Patient records were provided by Sichuan CDC [4], which curates a centralized database of hospitals records recording the information for all COVID-19 confirmed cases independently whether they required hospitalization. Our dataset covers the entire Sichuan Province, containing records from all hospitals in each prefecture of Sichuan. The dataset contains the following information for each case: age, sex, location of detection, exposure history, dates of symptom onset, date of hospital admission, date of official reporting, travel history in the last 14 days, clinical severity, and the reporting prefecture. The date of symptom onset was self-reported by the patient at the time of identification.

Performed interventions. All schools of Sichuan Province were closed on January 18, 2020. Sichuan declared the top-level public health emergency and established an emergency command center on January 24, 2020. Following this, gathering activities and entertainment (e.g., sports events) were suspended and public libraries closed. On January 26, the Sichuan government announced a strict set of measures to deal with the outbreak, including case isolation, tracing and screening of contacts of confirmed cases, quarantine of travelers from affected areas, and screening of people's temperature in public places. As of February 25, 2020, fourteen prefectures in Sichuan had no new confirmed cases for a week and the government decided to allocate provincial resources to deal with the epidemic in high-risk areas, while gradually starting to relax the interventions in medium and low-risk areas.

Statistical and modeling analysis

Descriptive statistics. We used the patient records to calculate the age distribution and gender of cases disaggregated by case severity. Further, we distinguished between locally acquired infections and those with travel history from Wuhan/Hubei. Cases with unknown travel history are considered as locally acquired infections. Additionally, we calculated distributions of time intervals from symptom onset to hospital admission and from symptom onset to reporting for those cases where all information was available.

Reproduction number. The basic reproduction number R_0 represents the mean number of secondary cases generated by a primary infector during the exponential growth phase of the epidemic, before interventions are applied and when the depletion of susceptible individuals is negligible [8]. The daily reproduction number $R(t)$ represents the mean number of secondary cases generated by a primary infector at time t [9]. The daily reproduction number is useful to track the effectiveness of performed control measures, which aims to push it below the epidemic threshold (corresponding to $R(t) = 1$). Moreover, $R(t)$ accounts for other factors affecting the spread of the epidemic such as the behavioral response of the population over time and the depletion of susceptible individuals in the population.

To estimate $R(t)$, we use the same methodology adopted by Zhang et al. [10], which was adjusted from [6,7] to distinguish between locally acquired and imported cases. Briefly, the number of locally acquired infections at time t depends on the transmissibility at time t (i.e., $R(t)$) and on the number of cases (both locally and imported as both contributes to the local transmission) at any time before t , weighted by the distribution of the generation time (which represents the time interval between consecutive generations of cases). The idea is that cases at a given time were generated by previous cases, proportional to the distribution of the generation time. The unknown parameter in this procedure is the transmissibility at time t as the

time series of cases and the distribution of the generation time are known. Formally, this estimation procedures work as follows. We assume that the daily number of new cases (date of symptom onset) with locally acquired infection $L(t)$ can be approximated by a Poisson distribution according to the renewal equation

$$L(t) \approx \text{Pois} \left(R(t) \sum_{s=1}^t \phi(s) C(t-s) \right),$$

where $C(t)$ is the number of new cases (either locally acquired or imported) at time t (date of symptom onset), $R(t)$ is the effective reproduction number at time t and ϕ is the generation time distribution. To estimate the time between consecutive generations of cases, we adopted the serial interval (which measures the time difference between the symptom onset of the infectors and of her/his infectees) estimated from the analysis of the first few clusters of COVID-19 cases detected in Wuhan before the implementation of the interventions, namely a gamma distribution with mean 7.5 days (shape = 4.87, rate = 0.65) [11].

The likelihood Λ of the observed time series cases from day 1 to T can be written as

$$\Lambda = \prod_{t=1}^T P(L(t), R(t) \sum_{s=1}^t \phi(s) C(t-s)),$$

where $P(x,y)$ is the Poisson density distribution of observing x events, given the parameter y .

We then use Metropolis-Hastings MCMC sampling to estimate the posterior distribution of $R(t)$. The Markov chains were run for 100,000 iterations, considering a burn-in period of 10,000 steps, and assuming non-informative prior distributions of $R(t)$ (flat distribution in the range (0–1000)). Convergence was checked by visual inspection by running multiple chains starting from different starting points. Finally, we use a 5-day moving average to visualize the trajectory of $R(t)$.

To estimate R_0 , we used the same equation adopted to estimate $R(t)$. Here, however, we estimated a constant daily reproduction number $R(t) = R_0$ over a time window early on in the outbreak and before the implementation of interventions [7]. Specifically, we estimated R_0 over the 1-week time window before the declaration of the outbreak, namely from January 18 to 24 and, when the outbreak was growing exponentially. In addition, as a sensitivity analysis, we estimated R_0 over a more conservative 2-week time window (from January 11 to 24, 2020).

Counterfactual scenarios. To estimate the number of cases averted by the policies implemented in Sichuan since the declaration of a public health emergency, we provided a set of counterfactual scenarios where we consider different starting dates of the interventions. To project the number of new COVID-19 cases (assuming a different starting date of the interventions), we use the renewal equation [7], which we already used to estimate the daily reproduction number. Essentially, the projected number of cases at a given time t depends on the reproduction number at time t and the number of cases (both locally acquired and imported as both contribute to the local transmission) at any time before t weighted by the distribution of the generation time. For the procedure to work, we need to know all these three ingredients. The projected number of new cases at time t can thus be formally estimated as:

$$C(t) = \text{Pois} \left(R(t) \sum_{s=1}^t \phi(s) C(t-s) \right),$$

where the notation is the same used in the previous section.

The proposed counterfactual scenarios consider a schematic representation of the dynamics of $R(t)$ that we have estimated for Sichuan (see Section Results). In particular, to mimic the estimated dynamics of $R(t)$, we assume $R(t) = R_0$ before the implementation of the control strategies; then we consider $R(t)$ to linearly decrease over a 1-week time window to its final constant value (R_{final}) estimated over the period from February 1 to the end of the epidemic.

Four counterfactual scenarios are considered, each one accounting for a different starting date of the interventions ranging from 1 week (January 31) to 4 weeks (February 21) after the actual declaration of the public health emergency from Sichuan health authorities on January 24. Each counterfactual scenario is based on 1,000 simulations, each one considering a value of R_0 and a value of R_{final} , sampled from the two estimated posterior distributions. It is important to stress that over the projection periods, the depletion of the susceptible population is negligible as compared with actual size of the Sichuan population (about 83,000,000 individuals [12]).

In addition to the main analysis described above, we consider two sensitivity analyses. In the first one, we consider a lower value of R_0 , as estimated over a 2-week time period before the declaration of the public health emergency. In the second one, instead of a linear decrease from R_0 to R_{final} , we consider an instantaneous switch between the two values occurring on the day when the public health emergency is declared. Such an instantaneous switch is different from what we estimated for Sichuan, but we decided to consider this additional scenario as there is no guarantee that, should the interventions be implemented at a later time, the dynamics of $R(t)$ would have been the same as the observed ones.

Averted cases. We define the number of averted cases as the difference between the final number of cases projected by the model and the actual number of reported cases. Similarly, we defined the number of averted severe and critical cases by multiplying the projected number of cases by the probability of developing severe or critical condition as estimated from the analysis of the patient records.

Results

Outbreak description

As of the March 16, 2020 a total of 539 cases were confirmed in Sichuan, including four asymptomatic subjects, 115 mild cases, 331 symptomatic cases, 57 severe cases, and 32 critical cases that required ICU treatment (Table 1). Among these confirmed cases, 253 had travel history from/to Wuhan/Hubei, 200 cases were locally acquired, and for the remaining 86 cases not known (Table 1 and Fig 1A). Thus, the Sichuan outbreak was characterized by a combination of local transmission and case importations.

The epidemic spread undetected in Sichuan Province until January 21, when the first COVID-19 case was identified. In the following days, 44 cases were identified to have symptom onset before that date (Fig 1B). The first symptomatic locally acquired case reported symptoms on January 10, a few days after the symptom onset of the first two detected cases with travel history from Wuhan. Up to January 30, the epidemic was mostly sustained by

Table 1. Characteristics of laboratory-confirmed COVID-19 cases in Sichuan disaggregated by case severity.

Characteristics/Case	Total	Mild	Symptomatic	Severe	Critical
Male—no./total no. (%)	285/539 (52.9%)	56/115 (48.7%)	177/331 (53.5%)	32/57 (56.1%)	17/32 (53.1%)
Median age (range)—years	45 (1–87)	36 (1–75)	45 (2–79)	48 (28–84)	64 (33–87)
Age group—no./total no. (%)					
0–19 years	34/539 (6.3%)	18/115 (15.7%)	15/331 (4.5%)	0/57 (0%)	0/32 (0%)
20–39 years	190/539 (35.1%)	46/115 (40.0%)	122/331 (36.9%)	16/57 (28.1%)	4/32 (12.5%)
40–64 years	255/539 (47.3%)	42/115 (36.5%)	170/331 (51.4%)	28/57 (49.1%)	13/32 (40.6%)
≥65 years	60/539 (11.1%)	9/115 (7.8%)	23/331 (7.0%)	13/57 (22.8%)	15/32 (46.9%)
Travel history to Wuhan/Hubei	253/539 (46.9%)	50/115 (43.5%)	168/331 (50.8%)	25/57 (43.9%)	10/32 (31.2%)

Notes. The total number of cases includes also 4 PCR positive asymptomatic individuals. Age and sex variables are available for all cases. Cases with unknown travel history are considered as locally acquired infections. Percentages might not total 100% because of rounding.

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imported cases (travel history to or from Wuhan or Hubei), with these peaking around January 23, just before the lockdown was imposed in Wuhan. After that date, we observe a steady decrease in imported cases and the opposite trend in local cases, showing evidence for sustained autochthonous transmission, peaking new local cases in February 8. After February 27, no new symptomatic cases were reported. The spatial distribution of cases was rather heterogeneous across the 21 prefectures of Sichuan, with Chengdu (the capital and most populous city) recording the largest number of cases at 144 (S1 Text and S1 Table).

The median age of the overall cases was 45 years (1–87) (Table 1). This median was higher in local cases (48 years, range: 1–87) than in imported cases (40 years, range: 2–81), see Table 2. A larger number of severe cases was found in older age groups (Table 1). Overall, the proportion of cases among individuals equal to 19 or younger than 19 years was 6.3%, with no severe or critical cases in that age group (Table 1).

Overall, the proportion of male cases is around 50% for all level of severity (Table 1). This slightly unbalanced proportion of male cases is more evident in imported cases (56.9%, Table 2), suggesting a larger fraction of travelers among males.

The mean time interval from symptom onset to hospital admission was estimated at 2.5 days (95% CI of the mean: 1.8–3.2, n = 153). By considering only cases reported before the declaration of the public health emergency, the mean was estimated at 3.2 days (95% CI of the mean: 1.2–5.3, n = 17) and 2.4 days (95% CI of the mean: 1.7–14.0, n = 136) thereafter; the variation between the two periods is not significant (two-sided t-test: p = 0.47). This mean time interval from symptom onset to reporting was estimated at 5.0 days (95% CI of the mean: 4.6–5.3, n = 535). Before the declaration of the public health emergency the mean time interval

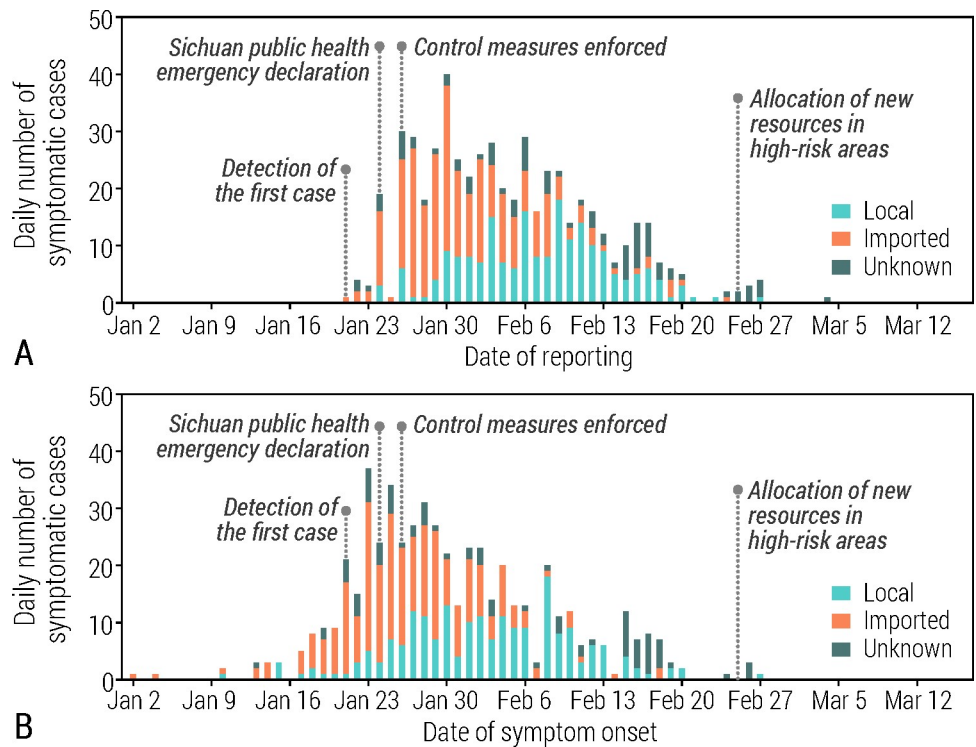


Fig 1. A Daily number of new symptomatic cases in Sichuan by date of reporting, disaggregated into cases with travel history to Wuhan/Hubei (imported), cases resulting from local transmission (local), and those for whom the travel history was unknown (unknown). **B** Same as A, but by date of symptom onset.

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Table 2. Characteristics of laboratory-confirmed COVID-19 cases in Sichuan province disaggregated by locally acquired infections and infected individuals with travel history to Wuhan/Hubei.

Characteristics	Imported cases	Local cases
Median age (range)—years	40.0 (2–81)	48.0 (1–87)
Age group—no./total no. (%)		
0–19 years	17/253 (6.7%)	12/200 (6.0%)
20–39 years	103/253 (40.7%)	58/200 (29.0%)
40–64 years	120/253 (47.4%)	99/200 (49.5%)
≥65 years	13/253 (5.1%)	31/200 (15.5%)
Case severity		
Mild	50 (19.8%)	46 (23.0%)
Symptomatic	168 (66.4%)	119 (59.5%)
Severe	25 (9.9%)	24 (12.0%)
Critical	10 (4.0%)	10 (5.0%)
Male—no./total no. (%)	144/253 (56.9%)	97/200 (48.5%)

Notes. Age and sex variables are available for all cases. Cases with unknown travel history are considered as locally acquired infections. Percentages might not total 100% because of rounding.

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from symptom onset to reporting was estimated at 5.4 days (95% CI of the mean: 3.5–7.3, $n = 27$) and at 4.9 days (95% CI of the mean: 4.5–5.3, $n = 508$) thereafter; the variation between the two periods is not significant (two-sided t-test: $p = 0.62$).

Reproduction number

Led by the first few imported cases from Wuhan/Hubei, we estimated the daily reproductive number to be well above the epidemic threshold at the beginning of the outbreak in Sichuan (Fig 2). The mean basic reproduction number R_0 was estimated at 2.4 (95% CI: 1.6–3.7) over the period from January 18 to January 24. This figure becomes 2.1 (95% CI: 1.6–2.7) if we consider the 2-week period of exponential growth from January 11 to January 24.

We estimated that the mean $R(t)$ above the epidemic threshold for about 2.5 weeks from January 10 to 27. From the declaration of the public health emergency in Sichuan, the estimated $R(t)$ continued to decline with a mean crossing the epidemic threshold on January 27, 3 days after the declaration. Since then, $R(t)$ was estimated to fluctuate constantly below the epidemic threshold (Fig 2). A similar temporal pattern of $R(t)$ was estimated for Chengdu as well with the exception of a final small resurgence of a few cases that led $R(t)$ above the unit for four days in late February (S1 Text and S3 Fig).

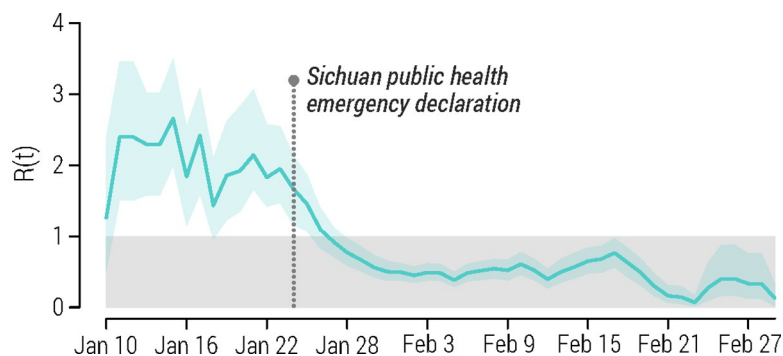


Fig 2. Estimated daily reproduction $R(t)$ (mean and 95% CI) over a 5-day moving average.

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Averted cases

Were the public health emergency been declared one week later, we estimated that the epidemic would have lasted about one week longer. However, were the declaration been done four weeks later, we estimated a non-linear effect, with an epidemic lasting 49 days longer (95% CI: 31–68 days) and the last case reported on April 19 (95% CI: April 1–May 10) (Fig 3).

The final mean number of projected cases was estimated to be between 775 (95% CI: 478–1,113) in the scenario where interventions started one week later than the actual date and 9,755 (95% CI: 1,856–26,084) in the scenario considering a 4-week delay. The estimated mean number of averted cases ranged from 236 (95% CI: -61-574), including 24 (95% CI: -6-60) severe and 14 (95% CI: -3-34) critical cases to 9,216 (95% CI: 1,317–25,545) cases, including 974 (95% CI: 139–2,701) severe cases, 547 (95% CI: 78–1,516) critical cases (Fig 3).

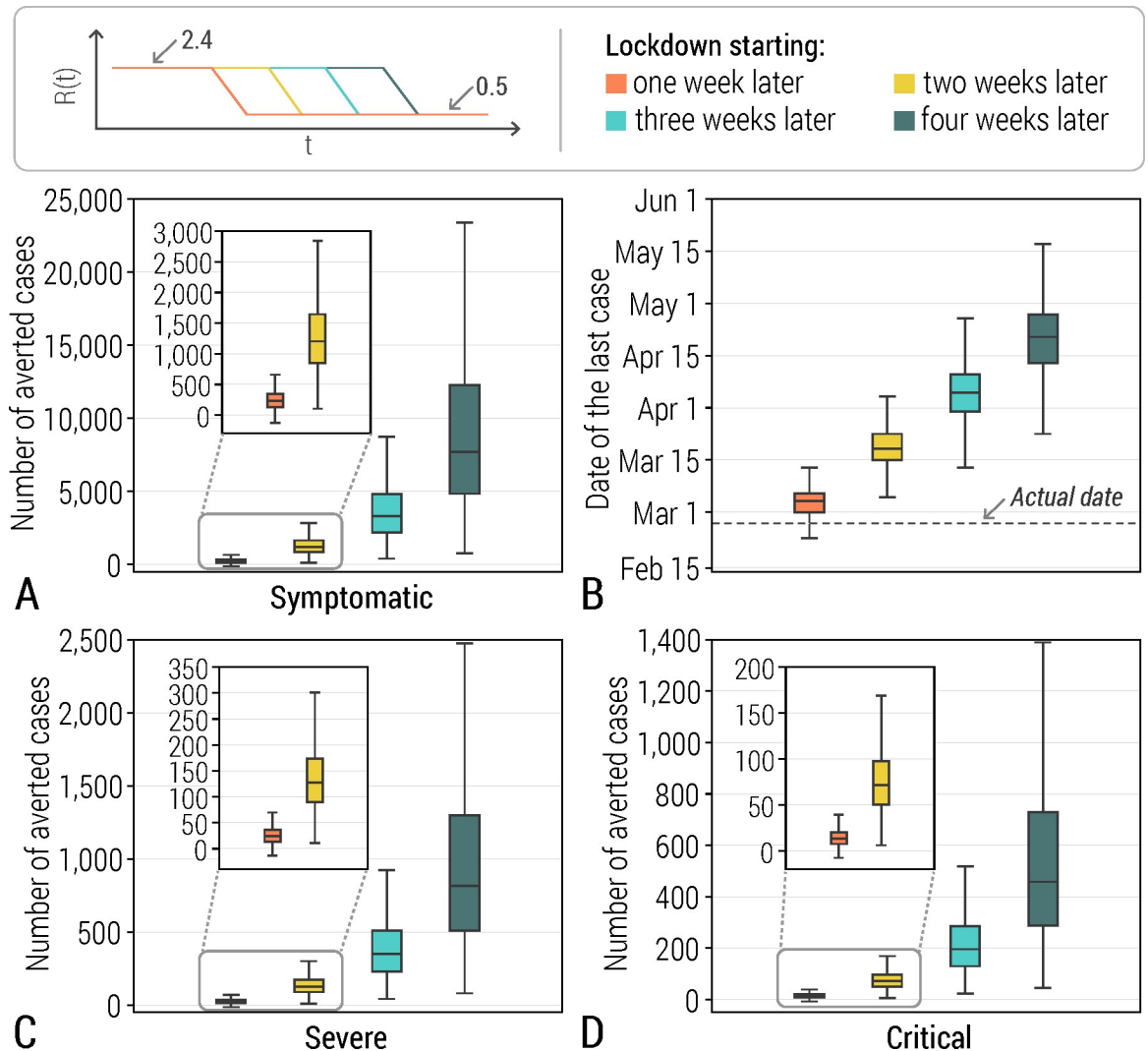


Fig 3. **A** Estimated number of averted symptomatic cases (min, quantile 0.25, median, quantile 0.75, max), should the public health declaration have occurred one to four weeks later. Estimates are obtained by considering $R_0 = 2.4$ (95% CI: 1.6–3.7) and $R_{final} = 0.47$ (95% CI: 0.4–0.54); $R(t)$ is assumed to follow a 1-week linear decrease from R_0 to R_{final} . R_{final} was estimated over the period from February 1 (i.e., one week after the declaration of the emergency) to the end of the outbreak. **B** Same as A, but for the date of the last case of the simulated epidemics. **C** Same as A, but for severe cases. **D** Same as B, but for critical cases.

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By considering a more conservative estimate of R_0 (2.1, 95% CI: 1.6–2.7) as obtained by considering a 2-week period of exponential growth at the beginning of the outbreak, we estimate the mean number of averted cases at 4,754 (95% CI: 1,138–12,104) in the scenario considering a 4-week delay in the declaration of the public health emergency (S1 Text and S4 Fig). In another sensitivity analysis where we considered an instantaneous decrease of SARS-CoV-2 transmissibility from R_0 to R_{final} occurring at the date of the declaration of the public health emergency, we estimated the mean number of averted cases at 6,701 (95% CI: 1,097–17,349) should the public health emergency be declared 4 weeks after the actual date (S1 Text and S5 Fig).

Discussion

We provided a characterization of the COVID-19 epidemiology in Sichuan Province of China. The outbreak accounted for a total of 539 PCR positive subjects and was characterized by a combination of local transmission and case importations. We estimated that SARS-CoV-2 transmissibility was above the epidemic threshold for about 4 weeks and then quickly declined after the declaration of a public health emergency in the province and the implementation of strict control measures. We found clear positive effects of the interventions implemented in Sichuan, possibly in combination with an increased awareness of the population about the epidemic spread, which achieved the interruption of transmission leading to a dramatic reduction of the COVID-19 burden in Sichuan.

With a total of 539 confirmed cases, Sichuan was able to successfully contain the COVID-19 outbreak. The epidemic started due to the importation of cases from Wuhan/Hubei. Then, we found a clear relationship between the lockdown of Hubei province, with only a handful of cases were imported from Wuhan/Hubei since early February. We observe a disproportionate fraction of COVID-19 cases being male in imported cases. This result indicates potential differential exposure by sex occurring at the beginning of the epidemic (e.g., sex difference among travelers) and is in overall in line with [13,14], where no significant difference in the risk of infection by gender was found. Nonetheless, it is important to stress that there are several limitations to our characterization of the COVID-19 outbreak in Sichuan that are related to investigation of rapidly evolving novel epidemics, such as biases in the detection of the first few cases, reporting rate, and unknown specifics of a novel pathogen.

In agreement with previous studies focusing on the spread of COVID-19 in China [10,11,13,14], we found a disproportionately low fraction of cases among individuals younger than 20 years as compared to the age structure of the population. From the data available here, it is not possible to ascertain whether younger individuals have a reduced risk of infection or an increased propensity for a milder clinical outcome of infection (thus resulting in a lower rate of detection). Both hypotheses were already discussed in [15] and found support in empirical epidemiological studies [16,17]. Nonetheless, it has to be taken into account that for the most of the epidemic, schools have been closed, at first due to the new year celebrations and then as a measure to control the epidemic spread [3]. Zhang and colleagues [16] showed that children recorded the largest number of contacts among all age groups on a regular weekday due to contacts at schools pre COVID-19, but this was largely reduced after the closure. It is uncertain if nationwide school holidays affected the small proportion of symptomatic cases among school-age individuals. Our approach of documenting the proportion of cases by age and severity does not allow us to readily tease apart the relative roles of age in susceptibility but leaves open opportunity for further scrutiny regarding potential drivers or risk factors that might lead to cohort effects of susceptibility to severe disease. The time interval from symptom onset to hospital admission and from symptom onset to reporting were estimated to be consistent with those reported in [10].

In the early phase of the outbreak, the daily reproduction number was essentially led by the first few imported cases from Wuhan/Hubei and we estimated the basic reproduction number to be in the ballpark of previous studies about COVID-19 spread in China [11,18–21]. We estimated that the daily reproduction number have followed a decreasing pattern before the declaration of the public health emergency by Sichuan authorities, although our results show that this pattern was not present at the local scale of Chengdu. This decreasing trend may possibly be linked to the increased awareness of the population of the ongoing COVID-19 epidemic in Wuhan and other areas of China. In fact, it has become apparent that individual and collective human behavior has had subtle and recognizable effects on SARS-CoV-2 transmission [22–25]. After the declaration of the public health emergency on January 24 and the adoption of strict control measures, we estimated a quick reduction of daily reproduction number, similar to what observed in other provinces of China [10] and elsewhere [26–29]. It is important to stress that the case definition changed over the course of the epidemic and, in particular, it was broadened on January 27 to include milder cases [30]. As such, it is possible that we are slightly overestimating the daily reproduction number since then and thus underestimating the beneficial effect of the interventions and population awareness in lowering SARS-CoV-2 transmission potential. However, as shown in [10], the effect is probably not very noticeable. Moreover, it should be noted that the entire time series of COVID-19 cases analyzed in this study is likely affected by underreporting. In order to account for that, we have used the renewal equation both for the estimation of the reproduction number over time and to project cases in the counterfactual scenarios, as this approach provides estimates that are robust to essentially any level of reporting [6,10]. To show that in the context of the COVID-19 outbreak in Sichuan, we have added two sensitivity analyses showing that both the estimated $R(t)$ and the estimated number of averted cases are robust to assuming reporting rates in the range 1%–100% (S1 Text and S1 and S2 Figs). Finally, it is also important to stress that the methodology adopted to estimate $R(t)$ assumes a well mixed population. In the case of high spatial variability, this hypothesis may not hold. Here, when analyzing the most affected prefecture of Sichuan (Chengdu), we estimated $R(t)$ to have a similar quantitative trend to that estimated for the entire Sichuan, providing support our findings.

We found that the implemented control strategies and population awareness have been highly effective in greatly limiting the burden of COVID-19. In particular, should the health authorities waited four weeks longer to declare the public health emergency, the epidemic would lasted more than six weeks longer and the number of cases would have been of the order of several thousands. It is important to stress that this figure would be much larger if we consider the number of infections instead of cases. In fact, asymptomatic individuals represent a sizable share of SARS-CoV-2 infected individuals [31,32]—up to 73.9% of the infected individuals aged less than 60 years developed neither fever nor respiratory symptoms according to Poletti and colleagues [17]. The evaluation of alternative strategies better targeting asymptomatic individuals is beyond the scope of this work.

It is important to stress that, to estimate the number of averted cases, we assumed that, before the detection of the outbreak, the epidemic would have continued its spread with the same basic reproduction number estimated during the initial exponential growth phase of the epidemic. It is however possible that, even if the public health emergency were not timely declared in Sichuan, the population could have adopted significantly different behaviors based on the knowledge that the epidemic was spreading in other areas of China. Moreover, the renewal equation approach is extremely simple and does not account for all the details of the mechanisms of SARS-CoV-2 transmission, such as the influx of imported cases or the underlying structure of the contact network of the population. In particular, we assumed that the distribution of cases by severity would have remained unchanged with respect to that estimated

in the early phase of the outbreak. This may have not been the case had the age-distribution of cases changed over time or had healthcare system been overwhelmed. Moreover, we did not account for the depletion of susceptible individuals in the population. However, since we projected cases in a short time window (a few weeks), the depletion of susceptible individuals is negligible and we do not expect to observe dramatic changes in the age distribution of cases over such a short time frame.

In conclusion, our results show the success in control strategies and adaptive behavioral changes of the population were instrumental in interrupting the SARS-CoV-2 transmission in Sichuan Province and preserved the healthcare system from a possible disruptive failure due to overwhelming stress imposed by the large number of severe and critical COVID-19 cases. Nevertheless, it is important to remark that the COVID-19 pandemic is far from being controlled at the global scale as we are still far from herd immunity and large proportion of the population remains susceptible. Thus, the course of the pandemic will rely on the efficiency of control strategies and individual behavior in the foreseeable future.

Supporting information

S1 Fig. Estimated mean daily reproduction $R(t)$ over a 5-day moving average for different values of the reporting rate ranging from 1% to 100%.

(PDF)

S2 Fig. Sensitivity analysis considering different reporting rates. **A** Estimated number of averted reported symptomatic cases (min, quantile 0.25, median, quantile 0.75, max), should the public health declaration have occurred four weeks later. Estimates are obtained by considering $R_0 = 2.4$ (95% CI: 1.6–3.7) and $R_{\text{final}} = 0.47$ (95% CI: 0.4–0.54); $R(t)$ is assumed to follow a 1-week linear decrease from R_0 to R_{final} . R_{final} was estimated over the period from February 1 (i.e., one week after the declaration of the emergency) to the end of the outbreak. Projections are obtained assuming four different values of the reporting rate, namely 1%, 10%, 50%, and 100%. **B** Same as **A**, but for the date of the last reported case of the simulated epidemics. **C** Same as **A**, but for severe cases. **D** Same as **B**, but for critical cases.

(PDF)

S3 Fig. Estimated daily reproduction $R(t)$ (mean and 95% CI) in Chengdu over a 5-day moving average.

(PDF)

S4 Fig. Sensitivity analysis considering R_0 , as estimated over a 2-week time period before the declaration of the public health emergency. **A** Estimated number of averted cases (min, quantile 0.25, median, quantile 0.75, max), should the public health declaration have occurred one to four weeks later. Estimates are obtained by considering $R_0 = 2.1$ (95% CI: 1.6–2.7) and $R_{\text{final}} = 0.47$ (95% CI: 0.4–0.54); $R(t)$ is assumed to follow a 1-week linear decrease from R_0 to R_{final} . R_{final} was estimated over the period from February 1 (i.e., one week after the declaration of the emergency) to the end of the outbreak. **B** Same as **A**, but for the date of the last case of the simulated epidemics. **C** Same as **A**, but for severe cases. **D** Same as **B**, but for critical cases.

(PDF)

S5 Fig. Sensitivity analysis considering an instantaneous drop from R_0 to R_{final} . **A** Estimated number of averted cases (min, quantile 0.25, median, quantile 0.75, max), should the public health declaration have occurred one to four weeks later. Estimates are obtained by considering $R_0 = 2.4$ (95% CI: 1.6–3.7) and $R_{\text{final}} = 0.53$ (95% CI: 0.47–0.60); $R(t)$ is assumed to instantaneously drop from R_0 to R_{final} . R_{final} was estimated over the period from January 25

(i.e., the day after the declaration of the emergency) to the end of the outbreak. B Same as A, but for the date of the last case of the simulated epidemics. C Same as A, but for severe cases. D Same as B, but for critical cases.

(PDF)

S1 Table. Total number of COVID-19 confirmed cases for each of the 21 prefectures of Sichuan Province of China.

(XLSX)

S1 Text. Additional results and sensitivity analyses.

(PDF)

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References

1. Tian H, Liu Y, Li Y, Wu CH, Chen B, Kraemer M, et al. An investigation of transmission control measures during the first 50 days of the COVID-19 epidemic in China. *Science*. 2020; 368(6491): 638–642. <https://doi.org/10.1126/science.abb6105> PMID: 32234804
2. Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature*. 2020; 584: 257–261. <https://doi.org/10.1038/s41586-020-2405-7> PMID: 32512579
3. Tu W, Tang H, Chen F, Wei Y, Xu T, Liao K, et al. Epidemic Update and Risk Assessment of 2019 Novel Coronavirus-China. *China CDC Weekly*. 2020; 2(6):83–86.
4. Health Commission of Sichuan Province. Notice of the first imported novel coronavirus case confirmed by the national health and Health Commission in January 21st. 2020. Available from <http://wsjkw.sc.gov.cn/scwsjkw/gzbd01/2020/1/21/c5d37b61355348769e41f0e73b112c16.shtml> (accessed on 8 June 2020).

5. Health Commission of Sichuan Province. Update on novel coronavirus pneumonia in Sichuan province (released in June 2nd). 2020. Available from <http://wsjkw.sc.gov.cn/scwsjkw/gzbd01/2020/6/22/Ob2382c03f24424584d673cc73cface5.shtml> (accessed on 22 June 2020).
6. Cori A, Ferguson NM, Fraser C, Cauchemez S. A new framework and software to estimate time-varying reproduction numbers during epidemics. *Am. J. Epidemiol.* 2013; 178(9):1505–1512. <https://doi.org/10.1093/aje/kwt133> PMID: 24043437
7. WHO Ebola Response Team. Ebola virus disease in West Africa—The first 9 months of the epidemic and forward projections. *N. Engl. J. Med.* 2014; 371:1481–1495. <https://doi.org/10.1056/NEJMoa1411100> PMID: 25244186
8. Keeling M, Rohani P. *Modeling Infectious Diseases: In Humans and Animals.* Princeton University Press; 2008.
9. Liu Q-H, Ajelli M, Aleta A, Merler S, Moreno Y, Vespignani A. Measurability of the epidemic reproduction number in data-driven contact networks. *Proc. Natl. Acad. Sci. U. S. A.* 2018; 115:12680–12685. <https://doi.org/10.1073/pnas.1811115115> PMID: 30463945
10. Zhang J, Litvinova M, Wang W, Wang Y, Deng X, Chen X, et al. Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: a descriptive and modelling study. *Lancet Infect. Dis.* 2020; 3099:1–10. [https://doi.org/10.1016/S1473-3099\(20\)30230-9](https://doi.org/10.1016/S1473-3099(20)30230-9) PMID: 32247326
11. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N. Engl. J. Med.* 2020; 382:1199–1207. <https://doi.org/10.1056/NEJMoa2001316> PMID: 31995857
12. Sichuan Provincial Bureau of Statistics National Bureau of Statistics. 2018 Statistical Yearbook of Sichuan, 2018. China Statistics Press.
13. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect. Dis.* 2020; 3099:1–9. [https://doi.org/10.1016/S1473-3099\(20\)30287-5](https://doi.org/10.1016/S1473-3099(20)30287-5) PMID: 32353347
14. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *J. Am. Med. Assoc.* 2020; 323(13):1239–42.
15. Davies NG, Klepac P, Liu Y, Prem K, Jit M, CMMID COVID-19 working group, et al. Age-dependent effects in the transmission and control of COVID-19 epidemics. *Nature Med.* 2020; 26:1205–1211. <https://doi.org/10.1038/s41591-020-0962-9> PMID: 32546824
16. Zhang J, Litvinova M, Liang Y, Wang Y, Wang W, Zhao S, et al. Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China. *Science.* 2020; 368(6498): 1481–1486. <https://doi.org/10.1126/science.abb8001> PMID: 32350060
17. Poletti P, Tirani M, Cereda D, Trentini F, Guzzetta G, Sabatino G, et al. Probability of symptoms and critical disease after SARS-CoV-2 infection. *arXiv:2006.08471*[Preprint]. 2020. Available from: <https://arxiv.org/abs/2006.08471>
18. Maier BF, Brockmann D. Effective containment explains subexponential growth in recent confirmed COVID-19 cases in China. *Science.* 2020; 368(6492), 742–746. <https://doi.org/10.1126/science.abb4557> PMID: 32269067
19. Kucharski AJ, Russell T, Diamond C, Liu Yang, Edmunds J, Funk S, et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *Lancet Infect Dis.* 2020; 20(5): 553–558. [https://doi.org/10.1016/S1473-3099\(20\)30144-4](https://doi.org/10.1016/S1473-3099(20)30144-4) PMID: 32171059
20. Wu JT, Leung K, Bushman M, Kishore N, Niehus R, de Salazar PM, et al. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. *Nature Med.* 2020; 26(4):506–10.
21. Chinazzi M, Davis JT, Ajelli M, Gioannini C, Litvinova M, Merler S, et al. The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. *Science.* 2020; 368(6489)395–400. <https://doi.org/10.1126/science.aba9757> PMID: 32144116
22. Bento AI, Nguyen T, Wing C, Lozano-Rojas F, Ahn Y-Y, Simon K. Evidence from internet search data shows information-seeking responses to news of local COVID-19 cases. *Proc. Natl. Acad. Sci.* 2020; 117(21):11220–11222. <https://doi.org/10.1073/pnas.2005335117> PMID: 32366658
23. Cowling BJ, Ali ST, Ng TWY, Tsang TK, Li JCM, Fong MW, et al. Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. *Lancet Public Health.* 2020; 5(5):E279–E288. [https://doi.org/10.1016/S2468-2667\(20\)30090-6](https://doi.org/10.1016/S2468-2667(20)30090-6) PMID: 32311320
24. Nguyen TD, Gupta S, Andersen M, Bento A, Simon K, Wing C. Impacts of State Reopening Policy on Human Mobility. NBER Working Paper No. w27235. 2020. Available from: <https://ssrn.com/abstract=3609688>

25. Gupta S, Nguyen TD, Rojas FL, Raman S, Lee B, Bento A, et al. Tracking Public and Private Response To the Covid-19 Epidemic. NBER Working Paper No. W27027. 2020. Available from: <https://ssrn.com/abstract=3586158>
26. Riccardo F, Ajelli M, Andrianou X, Bella A, Manso MD, Fabiani M, et al. Epidemiological characteristics of COVID-19 cases in Italy and estimates of the reproductive numbers one month into the epidemic. medRxiv 2020.04.08.20056861 [Preprint]. 2020. Available from: <https://www.medrxiv.org/content/10.1101/2020.04.08.20056861v1>
27. Cereda D, Tirani M, Rovida F, Demicheli V, Ajelli M, Poletti P, et al. The early phase of the COVID-19 outbreak in Lombardy, Italy. arXiv: 2003.09320 [Preprint]. 2020. Available from: <https://arxiv.org/abs/2003.09320>
28. Badr HS, Du H, Marshall M, Dong E, Squire M, Gardner LM. Association between mobility patterns and COVID-19 transmission in the USA: a mathematical modelling study. *Lancet Infect Dis*. 2020; 20(11):1247–1254. [https://doi.org/10.1016/S1473-3099\(20\)30553-3](https://doi.org/10.1016/S1473-3099(20)30553-3) PMID: 32621869
29. Miller AC, Foti NJ, Lewnard JA, Jewell NP, Guestrin C, Fox EB. Mobility trends provide a leading indicator of changes in SARS-CoV-2 transmission. medRxiv 2020.05.07.20094441 [Preprint]. 2020. Available from: <https://www.medrxiv.org/content/10.1101/2020.05.07.20094441v1>
30. Chinese Center for Disease Control and Prevention. Epidemic update and risk assessment of 2019 Novel Coronavirus. 2020. Available from: <http://www.chinacdc.cn/yrdgz/202001/P020200128523354919292.pdf> (accessed on 18 February 2020).
31. Byambasuren O, Cardona M, Bell K, Clark J, McLaws ML, Glasziou P. Estimating the extent of true asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. medRxiv 2020.05.10.20097543 [Preprint]. 2020. Available from: <https://doi.org/10.1101/2020.05.10.20097543>
32. Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review. *Annals of Internal Medicine*. 2020; 173: 362–368. <https://doi.org/10.7326/M20-3012> PMID: 32491919