

MR. SHI ZHAO (Orcid ID : 0000-0001-8722-6149)

DR. LIN YANG (Orcid ID : 0000-0002-5964-3233)

DR. DAIHAI HE (Orcid ID : 0000-0003-3253-654X)

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**Decreased Case Fatality Rate of COVID-19 in the Second Wave: a study in 53 countries or regions**

Guihong Fan<sup>1</sup>, Zhichun Yang<sup>2</sup>, Qianying Lin<sup>3</sup>, Shi Zhao<sup>4,5</sup>, Lin Yang<sup>6</sup>, and Daihai He<sup>7,\*</sup>

1 Mathematics Department, Columbus State University, US

2 School of Mathematical College, Chongqing Normal University, Chongqing, China, 401331

3 Michigan Institute for Data Science, University of Michigan, Ann Arbor, MI, United States

4 JC School of Public Health and Primary Care, Chinese University of Hong Kong, Hong Kong SAR, China

5 Shenzhen Research Institute of Chinese University of Hong Kong, Shenzhen, China

6 School of Nursing, Hong Kong Polytechnic University, Hong Kong, SAR, China.

7 Department of Applied Mathematics, Hong Kong Polytechnic University, Hong Kong Special Administrative Region, China

\* Correspondence author: Daihai He, Department of Applied Mathematics, Hong Kong Polytechnic University, Hong Kong, China. E-mail: [daihai.he@polyu.edu.hk](mailto:daihai.he@polyu.edu.hk);

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*fan\_guihong@columbusstate.edu*

*yangzhch@126.com*

*qianying@umich.edu*

*zhaoshi.cmsa@gmail.com*

*l.yang@polyu.edu.hk*

*daihai.he@polyu.edu.hk*

Abstract: The raw case fatality rate (CFR, reported number of COVID-19 deaths divided by the number of cases) is an important indicator to quantify the severity or treatment efficacy. In many countries, the pandemic had two waves to date. To our knowledge, no studies have compared the CFR between the two waves. In this work, we report that of 53 countries or regions with the highest death tolls, 43 had lower CFR estimates in the on-going second wave than in the first wave. We discussed the possible reasons. Also, we compared the two-wave pattern of COVID-19 with those of influenza. Influenza activities in the pre-pandemic era provided an indicator for seasonality of climate in a country. The sharp drop in 2020 influenza activity is an indicator of the effects of social distancing.

#### *Main Text*

The ongoing COVID-19 pandemic has caused a serious health threat globally. Many countries have seen a wave pattern of reported cases, namely a second wave followed the first wave. To our knowledge, there are no studies to date to compare the case fatality rate between these two waves.

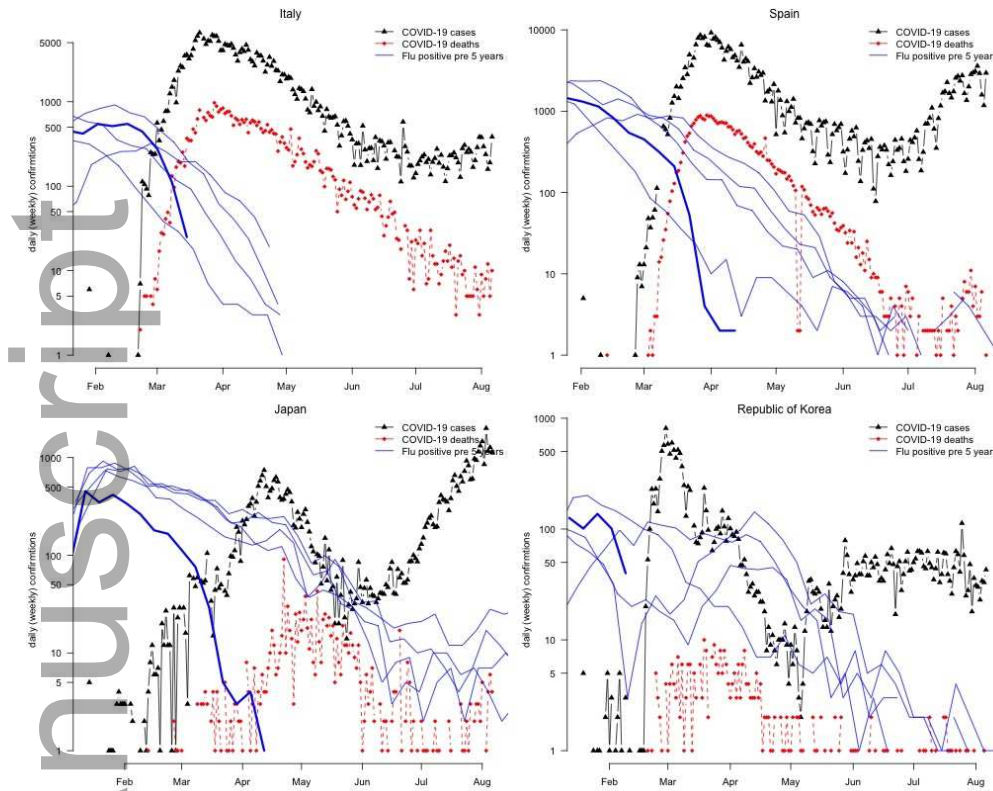


Figure 1. Time series plots of daily confirmed COVID-19 cases (in black), COVID-19 deaths (in red), and influenza positive cases in 2015-2019 (in light blue) and in 2020 (in dark blue).

We obtained the daily confirmations of COVID-19 cases and deaths for 216 countries or regions, during February 2020 - August 2020, and weekly influenza confirmations during 2015 to current week, from the World Health Organization [1,2]. We showed data of four countries (two from Europe and two from Asia which caught a lot of attention in the early phase of the pandemic) in Figure 1. Research of other 49 countries or regions are listed in the supplementary. The time series (in common log scale on vertical axis) of confirmed cases showed two waves. Based on this observation, we divided the transmission of the disease into two phases: Phase I before June 1 and Phase II after June 1 for confirmed cases; and Phase I before June 10 and Phase II after June 10 for deaths. For deaths, we choose the truncated time ten days later to account for the delay between confirmation and deaths [3]. We compared the raw case fatality rate (CFR) of Phase I and Phase II for all countries or regions.

In our supplementary data in the appendix, for each country, we break down the data for Phase I or Phase II. The column “case\_pre” is the total of confirmed cases before June 1 and the column

“case\_post” is the total of confirmed cases after June 1 up to July 26. Accordingly, the column of “death\_pre” is the infection death before June 10 and the column “death\_post” is the infection death after June 10 up to August 6. We define the raw case fatality rates (CFR) as  $r_1 = \frac{\text{death\_pre}}{\text{case\_pre}}$  and  $r_2 = \frac{\text{death\_post}}{\text{case\_post}}$ . Then the change in CFR is reduction =  $\frac{r_1 - r_2}{r_1}$ . Based on our analysis, among all 53 most affected countries or regions (supplementary Table 1), 43 had an apparent reduction in CFR, the rest ten had an increase in CFR in opposite. The median of the 53 reductions is 0.383 and the first quantile is 0.194. The decrease of CFR might indicate the decreasing severity of the global pandemic, and the potential reasons warrant further investigations. We propose the following hypotheses that could contribute to the decrease of CFR in the second phase. First, the lower CFR in the second phase than in the first phase could be a harvest effect. In other words, a large number of the elderly and those with health conditions (the vulnerable groups) likely had died in the first wave, especially in these countries with a high infection rate. By contrast, if a country or region (such as Hong Kong) was spared from the first phase, it might have an increase in CFR when the virus attacked again. Second, the test capacities and healthcare system in many countries could have been better prepared in the second phase. As a result, mild and asymptomatic cases were more likely reported in the later outbreaks, and severe cases could have received timely and treatments to greatly reduce the CFR. Third, the age structure of infected could have changed from the first wave to the second wave due to a variety of reasons, e.g. social movement in many countries might involve more healthier young individuals. Fourth, the virus might have evolved to increase its transmissibility in young healthy adults and children, which could be further facilitated by low compliance of social distancing in young people. Last but not least, favourable environmental factors might have led to a reduced CFR (e.g. warmer weather in the Northern Hemisphere and improved air quality due to city lockdown as reported in many studies [4-6]). The current evidence remains limited to suggest which of the above hypotheses is more plausible. Nevertheless, according to the classical epidemiologic triangle model, the interactions of the host, pathogen and environment determine the characteristics of outbreaks, rather than one or two factors alone.

We show the time series plots of eight countries in supplementary figures S1&S2, and summarizes the results of 53 countries or regions in supplementary figure S3, and Table 1. Majority of (43 out of 53) countries or regions had a decrease in the raw CFR. 10 countries

showed increased raw CFR, which could be due a variety of reasons, e.g. being in south hemisphere (Peru and Chile), milder first wave. The weekly influenza laboratory confirmations for the previous five years may be used as a proxy of the seasonality of climate and population global travel pattern in a country [7]. Thus we may wonder whether favourable weather may contribute to a reduce CFR for COVID-19. The sharp drop in influenza cases in 2020 (dark bold curve), compared to those in previous years, may be due to social distancing and possible interference with COVID-19 infection. Thus it is informative to compare the COVID-19 and influenza in these plots. Individual or age specific data are needed to further investigate the reasons behind changing CFR. The finding is nevertheless of significance to inform the public and policy makers. Although the lower CFR in the second phase is a positive sign to suggest the decrease severity of COVID-19 infections, the shift to younger age groups could bring more difficulty in containing the pandemic. We also need to stay vigilant for the potential rebound of influenza outbreaks as many countries or regions are planning to lift social distancing control measures.

### **Declarations**

### **List of abbreviations**

COVID-19: coronavirus disease 2019

CFR: case-fatality-rate

### **Ethics approval and consent to participate**

The ethical approval or individual consent was not applicable.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

All data and materials used in this work were publicly available.

### **Conflict of interests**

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### **Authors' Contributions**

All authors conceived the study, carried out the analysis, and drafted the first manuscript. All authors discussed the results, critically read and revised the manuscript, and gave final approval for publication.

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