Transmission potential of COVID-19 in Iran

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Abstract: n=50; Word limit = 50

We computed reproduction number of COVID-19 epidemic in Iran using two different methods. We estimated R_0 at 3.6 (95% CI, 3.2, 4.2) (generalized growth model) and at 3.58 (95% CI, 1.29, 8.46) (estimated epidemic doubling time of 1.20 (95% CI, 1.05, 1.44) days) respectively. Immediate social distancing measures are recommended.

Keywords: Communicable Diseases; Coronavirus; COVID-19; Epidemiology; Infections; Iran.

Iran has been experiencing an epidemic of COVID-19 (1). Since the first two cases were confirmed on February 19, 2020, a total of 593 cases have been reported as of February 29 (2). The virus appears to be spreading rapidly with cases reported among the elite (3). One model estimated that 18,300 (95% CI, 3,770 to 53,470) cases would have had occurred by February 24 (4). The Iranian authorities have adopted social distancing measures to slow disease transmission (5). As the epidemic continues, our results call for efforts to minimize COVID-19-related morbidity and mortality.

To confront the epidemic, we are interested in evaluating the transmission potential of COVID-19 to facilitate outbreak response efforts including the scope and intensity of interventions. The basic reproduction number, R_0, represents such a measurement indicating the average number of secondary cases that primary cases generate in a completely susceptible population in the absence of interventions or behavioral changes. $R_0>1$ indicated the possibility of sustained transmission, whereas $R_0<1$ implies that transmission chains cannot sustain epidemic growth. As the epidemic continues its course, the effective reproduction number offers a time-dependent record of the average number of secondary cases per case as the number of susceptible individuals gets depleted and control interventions takes effect. Herein we employed two different methods to quantify the reproduction number using the curve of reported COVID-19 cases.

Using a Wikipedia entry as a starting point, Farsi-speaking coauthor SFR double-checked the data of daily reported new cases, from February 19 through 29, 2020, using Iranian official press releases and other credible news sources, and corrected the data as per the official data. Two methods were utilized to estimate the reproduction number. The first method utilized a generalized growth model (GGM) (6) with the growth rate and its scaling factor to characterize the daily reported incidence, followed by simulation of the calibrated GGM, using a discretized probability distribution of the serial interval and assuming a Poisson error structure. See Technical Appendix for detailed description of data and Method 1.

The second method for estimating the reproduction number is based on the calculation of the epidemic's doubling times, which correspond to the times when the cumulative incidence doubles. We estimated the epidemic doubling time using the curve of cumulative daily reported cases. To quantify parameter uncertainty, we used parametric bootstrapping with a Poisson error structure around the number of new reported cases in order to derive 95% confidence intervals of our estimates. Assuming exponential growth, the epidemic growth rate is equal to ln(2)/doubling time. Assuming that the pre-infectious and infectious periods follow an exponential distribution, R_0 is approximately equal to 1 + growth rate $\times$ serial interval.

In both methods, the serial interval was assumed to follow a gamma distribution (mean: 4.41 days; standard deviation: 3.17 days) (7, 8). MATLAB version R2019b and R version 3.6.2 were used for data analyses and creating figures. It was determined *a priori* that $\alpha = 0.05$.

Using Method 1, we estimated a reproduction number of 3.6 (95% CI, 3.2, 4.2) for the COVID-19 epidemic in Iran. We estimated a growth rate of 0.85 (95% CI, 0.69, 1) and a scaling parameter of 0.89 (95% CI: 0.84, 0.95). The latter indicated a near-exponential growth of the epidemic (**Figure**). Using Method 2, we found that from February 19 through February 29, the cumulative incidence of confirmed cases in Iran had doubled 8 times. The estimated epidemic doubling time is 1.20 (95% CI, 1.05, 1.44) days and the corresponding R_0 estimate is 3.58 (95% CI, 1.29, 8.46).

Our study has limitations. First, it is based on the number of daily reported cases whereas it would be ideal to analyze case counts by date of symptom onset that are unavailable. Second, case counts could be underreported due to underdiagnosis, given subclinical or asymptomatic cases. The rapid increase in case count might represent a belated realization of the severity of the epidemic and a rapid process of catching up with testing many suspected cases. If the reporting ratio remains constant over the study period, and given the near-exponential growth of the epidemic's trajectory, our estimates would remain reliable; however, this is a strong assumption. Third, while data are not stratified according to imported and local cases, we assumed that they were infected locally, as it is likely that transmission has been ongoing in Iran for some time (4).

In conclusion, we used two different methods to compute the basic reproduction number of COVID-19 epidemic in Iran. Our mean estimate is at 3.6, which means that on average 3.6 susceptible individuals would be infected by one infectious individual. An epidemic trajectory of near-exponential growth raises serious concern. Our estimates provide further evidence that the epidemic situation in Iran is dire. Social distancing measures and prompt healthcare delivery need to be implemented swiftly.

Co-first authors' biographies

Kamalich Muniz-Rodriguez, a doctoral student in epidemiology, and Dr. Isaac Chun-Hai Fung, an associate professor of epidemiology, are at Jiann-Ping Hsu College of Public Health, Georgia Southern University. Their research interests include infectious disease epidemiology, digital health and disaster emergency responses.

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Conflict of interest statement

We do not have any conflict of interest to declare.

Disclaimer

This article does not represent the official positions of the Centers for Disease Control and Prevention, the National Institutes of Health, or the United States Government.

Ethics statement

The Georgia Southern University Institutional Review Board has made a non-human subjects determination for our project (H20364), under G8 exemption category.

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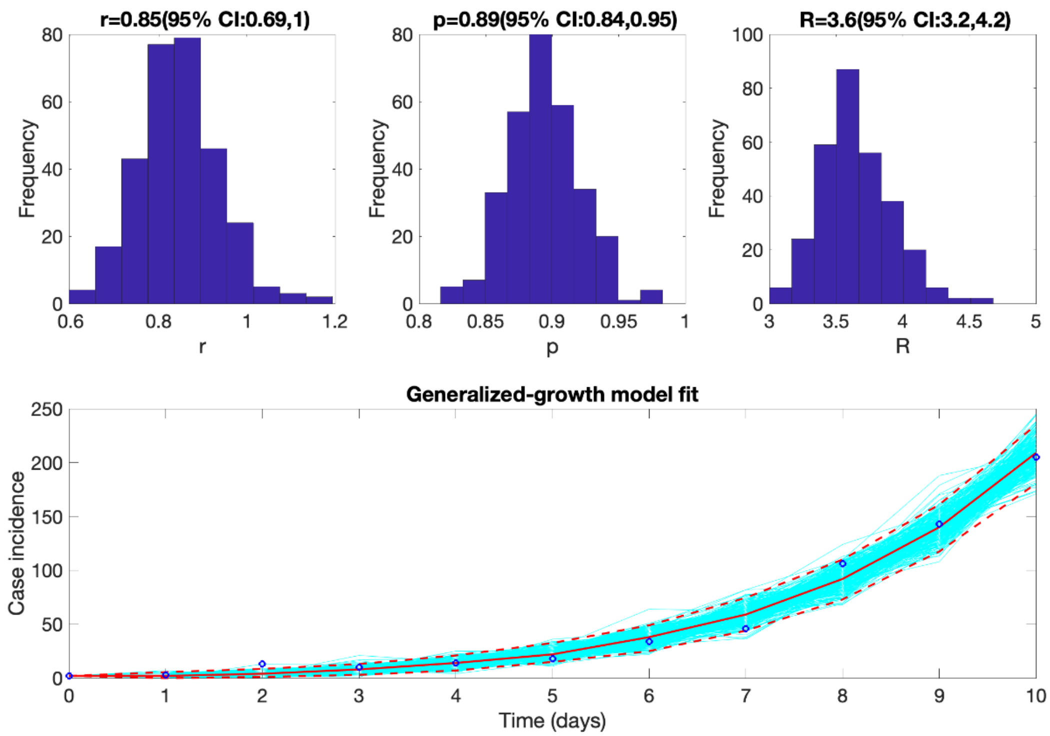
Figure. The mean effective reproduction number of COVID-19 epidemic in Iran, with 95% confidence interval. Estimates for growth rate, r, and the scaling of the growth rate parameter, p, are also provided. The plot in the lower panel depicts the fit of the Generalized Growth Model to the Iranian data assuming Poisson error structure as of February 29, 2020.



Transmission potential of COVID-19 in Iran

Technical Appendix

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Technical Appendix

Estimate of reproduction number from daily reported cases (Method 1)

Using the daily curve of reported cases in Iran, we estimate the reproduction number of COVID-19. For this purpose, we first characterize the daily reported incidence using the generalized growth model (GGM) (1). This model characterizes the growth profile via two parameters: the growth rate parameter (r) and the scaling of the growth rate parameter (p). The model captures diverse epidemic profiles ranging from constant incidence ($p = 0$), sub-exponential or polynomial growth ($0 < p < 1$), and exponential growth ($p = 1$) (1). The serial interval is assumed to follow a gamma distribution with a mean of 4.41 days and a standard deviation of 3.17 days based on recent reports (2, 3).

Next, to estimate the most recent estimate of R_t, we simulate the progression of incident reported cases from the calibrated GGM, and apply the discretized probability distribution (ρ_i) of the serial interval using the renewal equation (4-6) given by

$$R_{t_i} = \frac{I_i}{\sum_{j=0}^{i}(I_{i-j})\rho_i}.$$

In the renewal equation we denote the total incidence at calendar time t_i by I_i. Here, the denominator represents the total number of cases that contribute to the incidence cases at time t_i. Next, we estimate R_t from 300 simulated curves assuming a Poisson error structure to derive the uncertainty bounds around our estimate of the reproduction number (7).

Estimate of reproduction number from epidemic doubling times (Method 2)

We ran simulation to generate 10,000 sets of estimates of epidemic doubling times for a given time series of cumulative number of reported cases, and to compute the arithmetic mean of each set. Then, the harmonic mean of these estimates was calculated across 10,000 sets of simulations and was reported as our estimated epidemic doubling time, with 95% confidence interval (Table S2).

Next, we drew 10,000 random values for the serial interval from a gamma distribution with a mean of 4.41

days and a standard deviation of 3.17 days (2, 3). We generate 10,000 values for the reproduction number by calculating the reproduction number for each pair of values (arithmetic mean of epidemic doubling time and serial interval respectively) following the equation as in Vynnycky and White (8), Table 4.1, Equation 4.14:

$$\text{Reproduction number} = 1 + \text{growth rate} \times \text{serial interval}$$

We reported the mean and 95% of the 10,000 estimated values of the reproduction number (Table S2).

Results for Region 1 and Region 3 of Iran

In addition to estimating the reproduction number of COVID-19 across Iran, we further analyzed the data for Region 1 and Region 3 of Iran, which happened to have higher numbers of cumulative number of cases than other regions by February 29, 2020. Region 1 of Iran include Qom Province (QOM), Tehran Province (TEH), Mazandaran Province (MAZ), Alborz Province (ALB), Semnan Province (SEM), Golestan Province (GOL), and Qazvin Province (QAZ). Region 3 of Iran include Gilan Province (GIL), Ardabil Province (ARD), East Azerbajian Province (AZS), West Azerbajian Province (AZG), Kurdistan (or Kordestan) Province (KUR).

For Region 1, using Method 1, we estimated a reproduction number of 3.6 (95% CI: 3.1, 4.4) with a growth rate of 0.71 (95% CI: 0.54, 0.89) and a scaling parameter of 0.91 (95% CI: 0.85, 0.99). Using Method 2, the estimated epidemic doubling time was 1.29 (95% CI, 1.10, 1.61) and the estimated reproduction number was 3.40 (95% CI, 1.27, 7.91) (Table S2, Figures S1, S2 and S3).

For Region 3, using Method 1, we estimated a reproduction number of 3.0 (95% CI, 2.2, 4.2) with a growth rate of 0.96 (95% CI, 0.54, 1.6) and a scaling parameter of 0.80 (95% CI 0.63, 0.98). Using Method 2, the estimated epidemic doubling time was 1.30 (95% CI, 1.04, 1.78) and the estimated reproduction number was 3.38 (95% CI, 1.26, 8.04) (Table S2, Figures S1, S2 and S3).

It appeared that whether it was for Iran as a whole, or for its Region 1 or Region 3, the point estimate of the estimated reproduction number was 3.0 or higher. However, the estimates obtained from Method 1 had a smaller variance. The estimates obtained from Method 2 had a larger variance, given the large variance of the serial interval estimate that we used.

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Table S1. Cumulative number of daily reported number of new cases in Iran.

Date (yyyy-mm-dd)	Iran	Region 1	Region 3
2020-02-19	2	2	2
2020-02-20	5	4	2
2020-02-21	18	15	2
2020-02-22	28	25	2
2020-02-23	43	37	4
2020-02-24	61	48	6
2020-02-25	95	77	8
2020-02-26	139	98	18
2020-02-27	245	156	50
2020-02-28	388	254	82
2020-02-29	593	379	113

Region 1: Qom Province (QOM), Tehran Province (TEH), Mazandaran Province (MAZ), Alborz Province (ALB), Semnan Province (SEM), Golestan Province (GOL), Qazvin Province (QAZ).

Region 3: Gilan Province (GIL), Ardabil Province (ARD), East Azerbajian Province (AZS), West Azerbajian Province (AZG), Kurdistan (or Kordestan) Province (KUR).

Table S2. Estimated epidemic doubling time (95% Confidence intervals, CI), epidemic growth rate (95% CI) and the basic reproduction number (95% CI) obtained via Method 2. Epidemic growth rate (r) = ln(2)/doubling time. Basic reproduction number was calculated based on equation: R0 = 1 + growth rate × serial interval, assuming serial interval following a gamma distribution with a mean of 4.41 days and a standard deviation of 3.17 days.

	Estimated epidemic doubling times (95% CI)*	**Epidemic growth rate (r, 95% CI)**	**Basic reproduction number (95% CI) §**
Iran	1.20 (1.05, 1.44)	0.58 (0.66, 0.47)	3.58 (1.29, 8.46)
Region 1	1.29 (1.10, 1.61)	0.53 (0.63, 0.42)	3.40 (1.27, 7.91)
Region 3	1.30 (1.04, 1.78)	0.54 (0.67, 0.40)	3.38 (1.26, 8.04)

*Harmonic mean of the arithmetic means of 10,000 sets of simulated epidemic doubling times. §Calculated based on the 10,000 arithmetic means of 10000 sets of simulated epidemic doubling times and 10,000 random numbers drawn from a gamma distribution with a mean serial interval of 4.41 days (SD: 3.17 days).

Region 1: Qom Province (QOM), Tehran Province (TEH), Mazandaran Province (MAZ), Alborz Province (ALB), Semnan Province (SEM), Golestan Province (GOL), Qazvin Province (QAZ).

Region 3: Gilan Province (GIL), Ardabil Province (ARD), East Azerbajian Province (AZS), West Azerbajian Province (AZG), Kurdistan (or Kordestan) Province (KUR).

Figure S1. The mean effective reproduction number of COVID-19 in Region 1, Iran, with 95% confidence interval. Estimates for growth rate, r, and the scaling of the growth rate parameter, p, are also provided. The plot in the lower panel depicts the fit of the Generalized Growth Model to the Iranian data assuming Poisson error structure as of February 29, 2020.

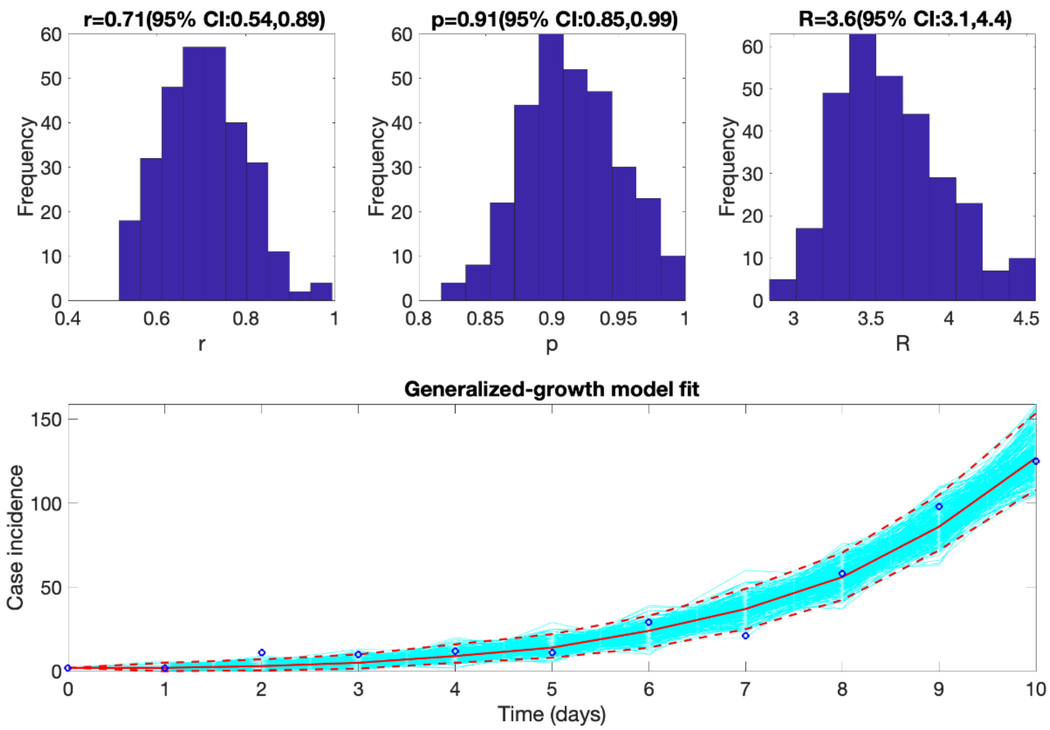


Figure S2. The mean effective reproduction number of COVID-19 in Region 3, Iran, with 95% confidence interval. Estimates for growth rate, r, and the scaling of the growth rate parameter, p, are also provided. The plot in the lower panel depicts the fit of the Generalized Growth Model to the Iranian data assuming Poisson error structure as of February 29, 2020.

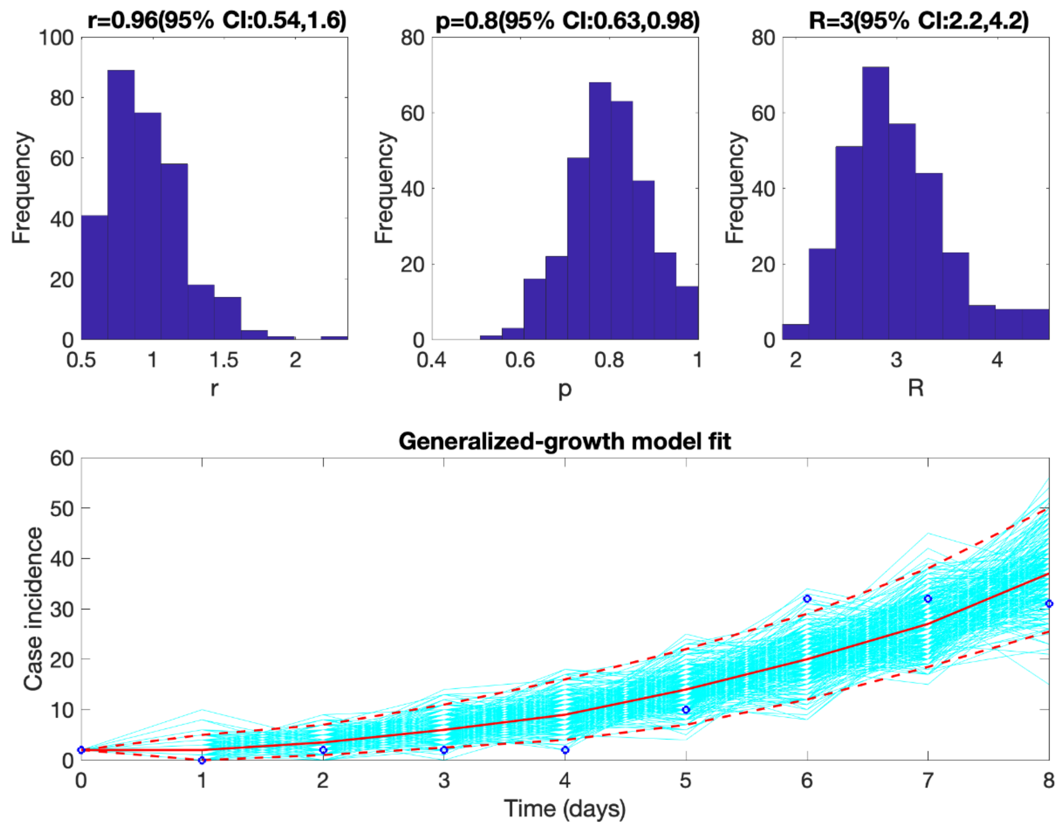
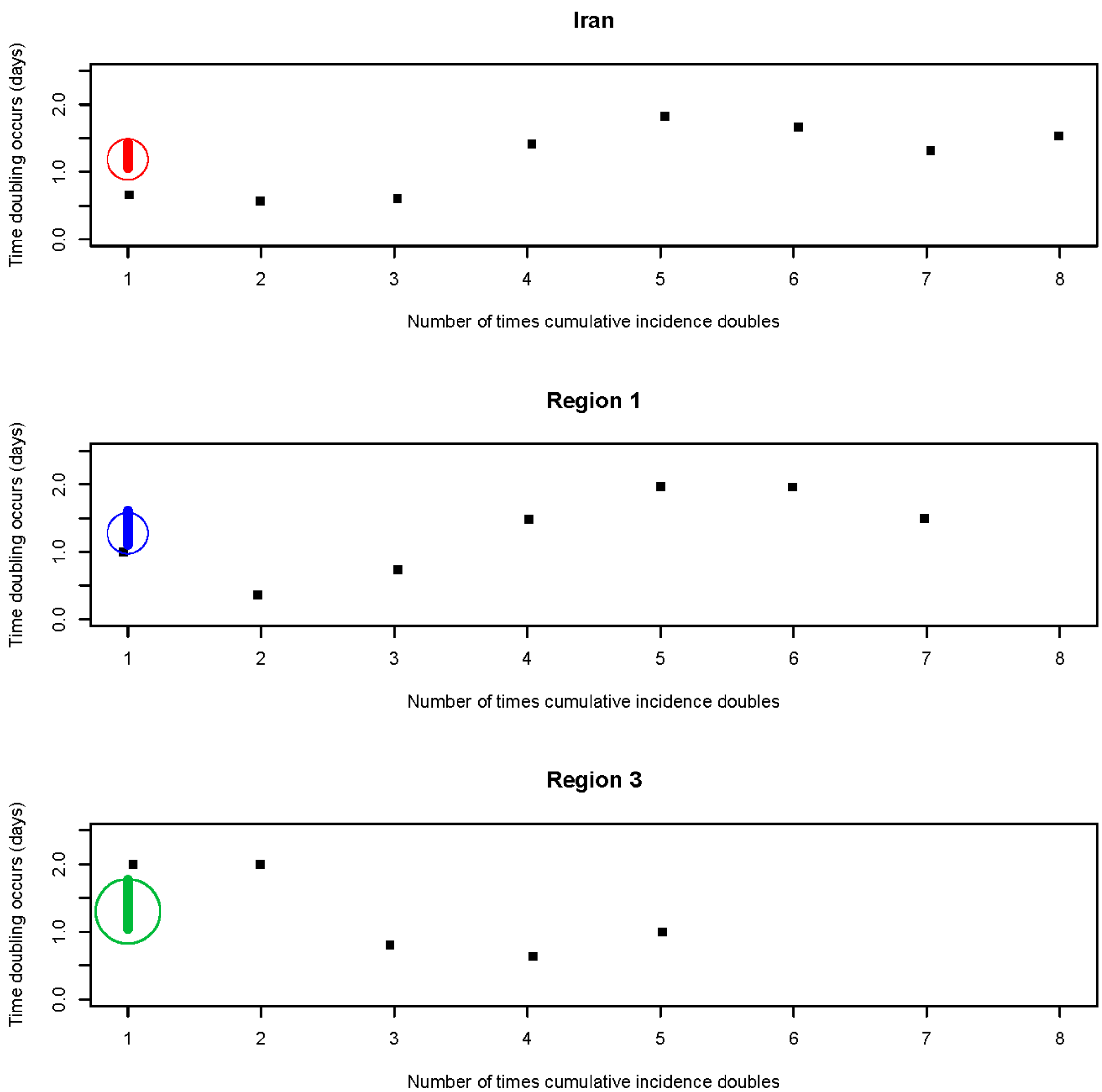


Figure S3. The COVID-19 epidemic doubling time (black square) and its harmonic mean with 95% confidence intervals (circle and bar) of Iran (upper panel, red) and the Iranian Region 1 (middle panel, blue) and Region 3 (lower panel, green).



Authors' contribution:

Conceptualization of the project: I. C. H. Fung and G. Chowell

MATLAB codes: G. Chowell

R codes: K. Muniz-Rodriguez and I. C. H. Fung

Data analysis (Method 1): G. Chowell

Data analysis (Method 2): K. Muniz-Rodriguez and I. C. H. Fung

Writing the first draft of the manuscript: I. C. H. Fung

Writing the section on Method 1 in Technical Appendix: G. Chowell

Manuscript editing: G. Chowell, I. C. H. Fung and K. Muniz-Rodriguez

Downloading Iranian official press releases and double-checking data: S. R. Ferdosi

Downloading news reports about COVID-19 epidemic in Iran: S. R. Ferdosi, S. K. Ofori,

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