# Modeling COVID-19: Forecasting and analyzing the dynamics of the outbreaks in Hubei and Turkey

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## Background

- In late 2019, the city of Wuhan in the province of Hubei, China experienced an outbreak of Coronavirus Disease 2019 (COVID-19).

- This outbreak quickly spread to all states of China and across the globe, being declared a pandemic by the World Health Organization (WHO) on 11 March 2020.

- Previous studies of COVID-19 provided the evidence of human-to-human transmission[2, 7, 18].

- Many (preprint) studies investigate dynamics of this pandemic from a global perspective (see, e.g., [8, 13, 14, 16, 19, 1]).

- Nevertheless, the large variations in both quality and availability of data from region to region lead us to bulild a new model.

## Flow diagram



Figure: Flow diagram illustrating the disease transitions among the compartments
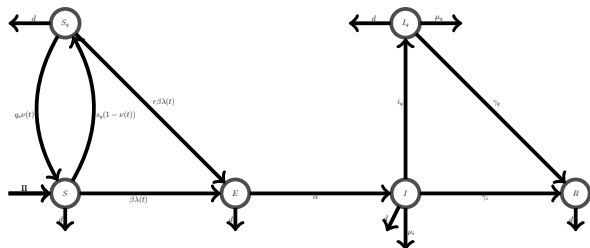
- $S$: Susceptible
- $S_q$: Susceptible, but in self-isolation
- $E$: Exposed
- $I$: Infected
- $I_q$: Infected and Isolated
- $R$: Recovered

where

$$\lambda(t) = \frac{I(t)}{N(t)} \quad \text{and} \quad \nu(t) = e^{-I_q(t)}$$

## Model formulation

$$\frac{dS(t)}{dt} = \Pi + q_s e^{-I_q(t)} S_q(t) - s_q(1 - e^{-I_q(t)})S(t) - \beta\lambda(t)S(t) - dS(t)$$

$$\frac{dS_q(t)}{dt} = s_q(1 - e^{-I_q(t)})S(t) - q_s e^{-I_q(t)} S_q(t) - r\beta\lambda(t)S_q(t) - dS_q(t)$$

$$\frac{dE(t)}{dt} = \beta\lambda(t)S(t) + r\beta\lambda(t)S_q(t) - \alpha E(t) - dE(t)$$

$$\frac{dI(t)}{dt} = \alpha E(t) - i_q I(t) - \gamma_i I(t) - \mu_i I(t) - dI(t) \qquad (1)$$

$$\frac{dI_q(t)}{dt} = i_q I(t) - \gamma_q I_q(t) - \mu_q I_q(t) - dI_q(t)$$

$$\frac{dR(t)}{dt} = \gamma_i I(t) + \gamma_q I_q(t) - dR(t)$$

with $S(0) > 0, S_q(0) \geq 0, E(0) \geq 0, I(0) \geq 0, I_q(0) \geq 0, R(0) \geq 0$ and
$N(t) = S(t) + S_q(t) + E(t) + I(t) + I_q(t) + R(t)$

# Parameters

Table: Parameter descriptions and values

| Parameter | Description | Value | Unit | Source |
|---|---|---|---|---|
| $\mathcal{R}_0$ | The basic reproduction number | 5.49 | - | Estimated |
| $\beta$ | Disease transmission rate | 5.24 | $\frac{1}{day}$ | Estimated |
| $q_s$ | Rate of release from quarantine | 0.5 | $\frac{1}{day}$ | Estimated |
| $s_q$ | Quarantine rate of susceptible individuals | 0.096 | $\frac{1}{day}$ | Estimated |
| $\alpha$ | Rate of exposed individuals becoming infected | 0.2381 | $\frac{1}{day}$ | [12, 6, 15] |
| $\gamma_i$ | Recovery rate due to natural immune response | 0.111 | - | Estimated |
| $\gamma_q$ | Recovery rate due to hospitalization | 0.107 | $\frac{1}{day}$ | Estimated |
| $\mu_i$ | Death rate of disease in infectious compartment | 0.0096 | $\frac{1}{day}$ | Estimated |
| $\mu_q$ | Death rate due to disease in reported infectious compartment | 0.004 | $\frac{1}{day}$ | Estimated |
| $\iota_q$ | Rate of reported (infected) individuals | 0.832 | $\frac{1}{day}$ | Estimated |
| $r$ | Reduction rate in transmission due to quarantine | 0.011 | - | Estimated |
| $\Pi$ | Recruitment rate | 2134 | $\frac{Individual}{day}$ | [17] |
| $d$ | Natural death rate | 0.000023 | $\frac{1}{day}$ | [17] |
| $E(0)$ | Initial number of exposed Individuals | 142 | Individual | Estimated |
| $I(0)$ | Initial number of infected Individuals | 69 | Individual | Estimated |

## Diseases free equilibrium

One of major concepts in an outbreak is disease free equilibrium (DFE), where the entire population is susceptible [9, 3].

$$x^* = (S^*, S_q^*, E^*, I^*, I_q^*, R^*) = (S^*, 0, 0, 0, 0, 0).$$

To obtain the DFE for the system (1), we set the right hand side of the system (1) to zero and substitute the DFE into the system. Hence, the DFE is given by

$$x^* = (S^*, S_q^*, E^*, I^*, I_q^*, R^*) = (\frac{\Pi}{d}, 0, 0, 0, 0, 0).$$

## Stability analysis

For stability analysis of the DFE, we employ the next-generation matrix (NGM) [5, 3, 4]. After some calculations the NGM is given by

$$\mathbf{F}(\mathbf{X}^*)\mathbf{V}(\mathbf{X}^*)^{-1} = \begin{bmatrix} \frac{\alpha\beta}{(\alpha+d)(i_q+\gamma_i+\mu_i+d)} & \frac{\beta}{i_q+\gamma_i+\mu_i+d} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \qquad (2)$$

The spectral radius of the NGM is the basic reproduction number $\mathcal{R}_0$ defined to be the average number of secondary cases arising from an average primary infected case in an entirely susceptible population. The DFE is locally stable if $\mathcal{R}_0 < 1$ [5, 3]. $\mathcal{R}_0$ is given by

$$\rho(\mathbf{F}\mathbf{V}^{-1}) = \mathcal{R}_0 = \frac{\alpha\beta}{(\alpha+d)(i_q+\gamma_i+\mu_i+d)}$$

if

$$i_q > \frac{\alpha\beta}{(\alpha+d)} - \gamma_i - \mu_i - d$$

then the DFE is locally stable

## Data and model fit

The data are used in the model fit are the cumulative number of cases and the cumulative number of deaths. The goodness of the fit is measured by computing the associated relative error of the fit using the formula

$$\min \left( \frac{\sum_{i=1}^{n} (C_i - \hat{C}_l)^2}{\sum_{i=1}^{n} C_i^2} + \frac{\sum_{i=1}^{n} (D_i - \hat{D}_l)^2}{\sum_{i=1}^{n} D_i^2} \right) \approx 0.06 \tag{3}$$

where $C_i$ is the true value of cumulative number of cases and $\hat{C}_l$ is estimated cumulative number of cases. $D_i$ is the true value of cumulative number of deaths and $\hat{D}_l$ is estimated cumulative number of deaths.
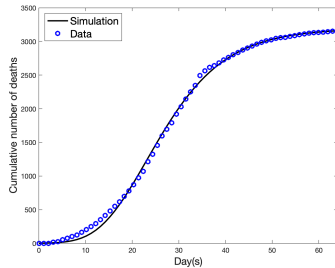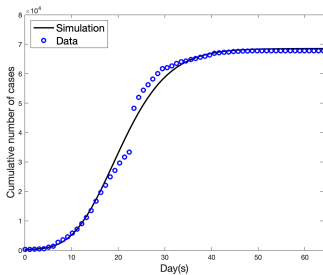
# Model fit



Figure: Fitting the model to the data from January 20, 2020 to March 23, 2020 in Hubei: the cumulative number of (infected) cases and deaths (Parameter values used are as given in Table 1 ).

## Sensitivity Analysis

In order to determine the set of parameters that are statistically significant with regard to the number of cumulative infected cases, we conduct a sensitivity analysis of the model. We utilized a Latin Hypercube Sampling (LHS) and the Partial Rank Correlation Coefficients (PRCC) method [10].

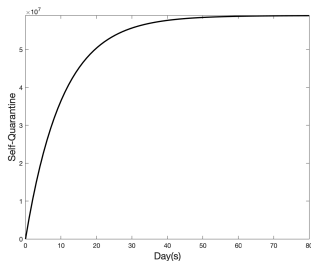| Parameter | PRCC | p-value | Range |
|-----------|------|---------|-------|
| $\beta$ | 0.89 | 1.2e-104 | [1, 10] |
| $q_s$ | -0.084 | 0.15 | [0.1, 0.9] |
| $s_q$ | -0.45 | 3.4e-16 | [0.01, 0.2] |
| $\alpha$ | 0.23 | 6.9e-05 | [0.05, 0.5] |
| $\gamma_i$ | -0.25 | 1.3e-05 | [0.01, 0.2] |
| $\gamma_q$ | -0.075 | 0.2 | [0.01, 0.4] |
| $\mu_i$ | -0.052 | 0.37 | [0.001, 0.2] |
| $\mu_q$ | 0.12 | 0.032 | [0.001, 0.2] |
| $i_q$ | -0.81 | 3.1e-70 | [0.5, 4] |
| $r$ | 0.69 | 8.3e-44 | [0.001, 0.9] |
| $\Pi$ | -0.05 | 0.39 | [0.01, 0.1] |
| $d$ | 0.067 | 0.25 | [0.000001, 0.0001] |

## Simulation of Self-isolation



Figure: Transitions from the susceptible class to the quarantine class during the outbreak in Hubei

The self-isolation reduces the contact rate by 98.9%. In addition, when we reduce the quarantine rate, $s_q$ by 10%, the number of cases and deaths would be about 141,090 and 6,562. Similarly, as we increase the quarantine rate, $s_q$ by 10%, the number of cases and deaths would be about 39,334 and 1,829. Thus, 10% change makes a double change in the number of deaths and cases

## Parameter estimation with Turkish data

We consider data from March 10, 2020 to April 10, 2020, and achieve a fit (see equation (3)) with approximately 5.9% relative error. We estimate the four parameters $i_q$, $s_q$, $\beta$, and $r$, which are not only the most significant parameters in the dynamics of outbreak, but also tend to be specific to each local region. Turkish data in [11] are used in the estimation. New estimates are as below

Table: Parameter descriptions and values of the model (1) with Turkish data.

| Parameter | Description | Value | Unit | Source |
|---|---|---|---|---|
| $\mathcal{R}_0$ | The basic reproduction number | 5.2 | - | Estimated |
| $\beta$ | Disease transmission rate | 9.98 | $\frac{1}{day}$ | Estimated |
| $s_q$ | Quarantine rate of susceptible individuals | 0.088 | $\frac{1}{day}$ | Estimated |
| $i_q$ | Rate of reported (infected) individuals | 1.8 | $\frac{1}{day}$ | Estimated |
| $r$ | Reduction rate in transmission due to quarantine | 0.15 | - | Estimated |
| $\Pi$ | Recruitment rate | 3827 | $\frac{Individual}{day}$ | [17] |
| $d$ | Natural death rate | 0.000016 | $\frac{1}{day}$ | [17] |
| $E(0)$ | Initial number of exposed Individuals | 6 | Individual | Estimated |
| $I(0)$ | Initial number of infected Individuals | 2 | Individual | Estimated |

## Simulation of self-isolation
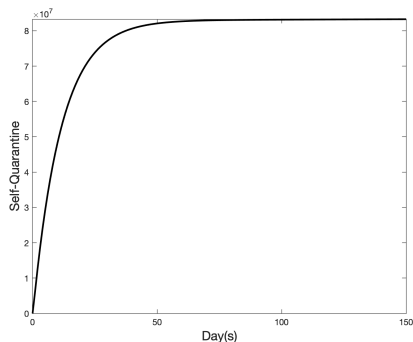


The efficiency of quarantine also seems to be very good in Turkey, given the approximately 85% reduction in the contact rate of COVID-19 obtained by our parameter estimation. On the other hand, the quarantine rate is about 0.088, which is small when compared with the quarantine rate in Hubei (the rate was 0.096). This may provide some insight into why the contact rate is higher in Turkey when compared to the contact rate in Hubei.

## Simulation, effect of self-isolation and the number of tests on the cumulative number of cases

One of novels of our model is indirectly to quantify the number of tests by using the parameter $i_q$. It is yet possible to increase the quarantine rate $s_q$ and the number of COVID-19 tests given each day by increasing the rate of reported cases $i_q$ in Turkey to see the effect of reduction in the number of cases and deaths.
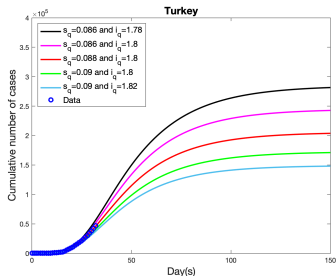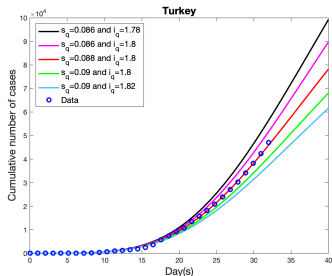


Figure: Cumulative number of (infected) cases depending on different quarantine rate $s_q$ and rate of reported cases $i_q$. The left plot shows the cumulative number of cases between day 1 to day 40, and right plot shows the cumulative number of cases between day 1 to day 150 in the outbreak in Turkey.

# Simulation, effect of self-isolation and the number of tests on the cumulative number of deaths
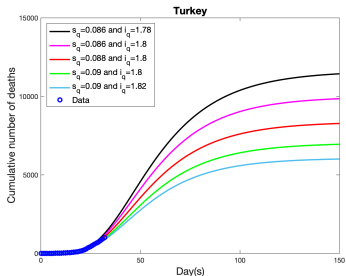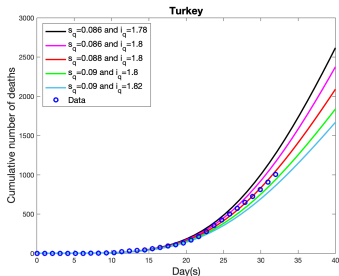


Figure: Cumulative number of deaths depending on different quarantine rate $s_q$ and rate of reported cases $i_q$. The left graph shows the cumulative number of deaths between day 1 to day 40, and right plot shows the cumulative number of deaths between day 1 to day 150 in the outbreak in Turkey.

## Simulation of the peak

The peak of the outbreak in Turkey is also very sensitive to the quarantine rate $s_q$ and the rate of reported cases $i_q$. Depending on the change in quarantine rate and the rate of reported cases $i_q$, the peak of outbreak in Turkey can be seen between the day 42 (April 20,2020) and day 48 (April 26, 2020), and the outbreak will almost die out by the day 150 (at the end of July 2020, see Figure 11).
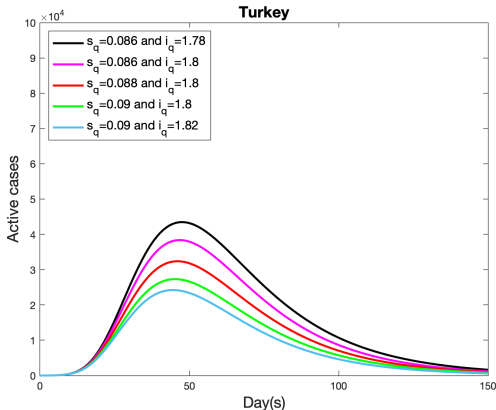


Figure: Projected (simulated) peak of outbreak in Turkey depending on different quarantine rate $s_q$ and rate of reported cases, $i_q$.

## Conclusion

- Our analysis suggests that quarantine greatly reduced the number of cases and deaths as seen in Hubei's COVID-19 outbreak. In addition, while quarantine does not appear in the representation of $\mathcal{R}_0$, it still indirectly reduces $\mathcal{R}_0$. Our sensitivity analysis also indicated that the dynamics of the outbreak are very sensitive to the quarantine rate $s_q$.

- Increasing (or decreasing) the speed of movement from the susceptible class to the quarantine class by about 10% would double (or half) the number of cases and deaths due to the outbreak (This speed of movement is the rate $s_q$).

- Of course, the efficiency of a quarantine (i.e., the level of social distancing) is also very important. In our model, the efficiency of the quarantine is measured by the reduction rate $r$. Our sensitivity analysis confirmed that this parameter is very important (see Figure 6).

- Another important parameter that plays a crucial role in the dynamics of the outbreak is the rate of reported cases $i_q$ which is directly related to the number of tests given to detect infected individuals.

📄 Zhidong Cao et al. "Estimating the effective reproduction number of the 2019-nCoV in China". In: *medRxiv* (2020).

📄 Jasper Fuk-Woo Chan et al. "A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster". In: *The Lancet* (2020).

📄 Odo Diekmann, JAP Heesterbeek, and Michael G Roberts. "The construction of next-generation matrices for compartmental epidemic models". In: *Journal of the Royal Society Interface* 7.47 (2010), pp. 873–885.

📄 P Van den Driessche and James Watmough. "Further notes on the basic reproduction number". In: *Mathematical epidemiology*. Springer, 2008.

📄 Pauline Van den Driessche and James Watmough. "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission". In: *Mathematical biosciences* 180.1-2 (2002), pp. 29–48.

📄 Wei-jie Guan et al. "Clinical characteristics of 2019 novel coronavirus infection in China". In: *MedRxiv* (2020).

📄 Chaolin Huang et al. "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China". In: *The Lancet* (2020).

📄 Natsuko Imai et al. *Estimating the potential total number of novel Coronavirus cases in Wuhan City, China*. 2020.

📄 M. J. Keeling and P Rohani. "Modeling Infectious Diseases in Humans and Animals". In: *Biometrics* 64.3 (2008), pp. 993–993. ISSN: 0006-341X.

📄 Simeone Marino et al. "A methodology for performing global uncertainty and sensitivity analysis in systems biology". eng. In: *Journal of Theoretical Biology* 254.1 (2008), pp. 178–196. ISSN: 0022-5193.

📄 Ministry of Health (Turkey). *Coronavirus Disease 2019 (COVID-19) daily data*. https://covid19.saglik.gov.tr. 2020.

📄 Hiroshi Nishiura, Natalie M Linton, and Andrei R Akhmetzhanov. "Serial interval of novel coronavirus (2019-nCoV) infections". In: *medRxiv* (2020).

📄 Jonathan M Read et al. "Novel coronavirus 2019-nCoV: early estimation of epidemiological parameters and epidemic predictions". In: *medRxiv* (2020).

📄 Julien Riou and Christian L Althaus. "Pattern of early human-to-human transmission of Wuhan 2019-nCoV". In: *bioRxiv* (2020).

📄 Steven Sanche et al. "The Novel Coronavirus, 2019-nCoV, is Highly Contagious and More Infectious Than Initially Estimated". In: *arXiv preprint arXiv:2002.03268* (2020).

📄 Mingwang Shen et al. "Modelling the epidemic trend of the 2019 novel coronavirus outbreak in China". In: *bioRxiv* (2020).

📄 World Health Organization. *Crude birth and death rate Data by country*. http://apps.who.int/gho/data/node.main.CBDR107?lang=en. 2020.

📑   Xintian Xu et al. "Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission". In: *Science China Life Sciences* (2020), pp. 1–4.

📑   Shi Zhao et al. "Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak". In: *International Journal of Infectious Diseases* (2020).