Predicting the Development of COVID-19 Epidemics from Reported Case Data

Glenn Webb

Vanderbilt University

October 5, 2020

Objectives:

1. Develop mathematical models to provide predictions for COVID-19 epidemics.
2. Incorporate asymptomatic and symptomatic infectiousness transmission.
3. Use reported case data to parameterise the models at the epidemic outbreak stage.
4. Use the models to project the epidemic forward with varying social distancing and public health measures.

Collaborators

Zhihua Liu, Beijing Normal University, China

Pierre Magal, University of Bordeaux, France

Ousmane Seydi, Ecole Polytechnical University, Senegal

Compartments of the model

1. $S(t)$ - susceptible population at time t
2. $I(t)$ - asymptomatic infectious population at time t
3. $R(t)$ - reported symptomatic infectious population at time t
4. $U(t)$ - unreported symptomatic infectious population at time t

Stages of the model

- Stage I: *The epidemic exponential stage. The cumulative number of reported cases increases exponentially before major social measures are implemented.*
- Stage II: *Major social measures are implemented. The number of transmissions decreases significantly. Transmissions are due to asymptomatic infectiousness and symptomatic infectiousness of unreported cases.*
- Stage III: *Major social measures are relaxed. The number of transmissions increases. Transmissions are due primarily to asymptomatic infectiousness.*

Parameters of the model

1. Susceptibles become infected from asymptomatically infectious and symptomatically infectious individuals at rate $\tau(t, S(t), I(t), U(t))$.

2. Asymptomatic infectious individuals $I(t)$ are infectious for an average period of $1/\nu$ days.

3. Reported symptomatic individuals $R(t)$ are infectious for an average period of $1/\eta$ days, as are unreported symptomatic individuals $U(t)$

4. A fraction f of asymptomatic infectious become reported symptomatic infectious at rate $\nu_1 = f\,\nu$, and a fraction $1 - f$ become unreported symptomatic infectious at rate $\nu_2 = (1 - f)\,\nu$, where $\nu_1 + \nu_2 = \nu$.

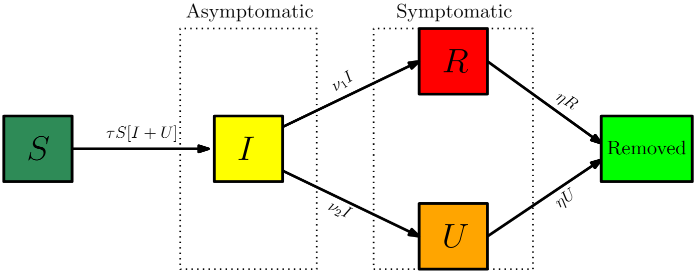


Figure : Flow diagram of the model.

Equations of the model

$$
\begin{aligned}
S'(t) &= -\tau(t, S(t), I(t), U(t))\; t \geq t_0,\\
I'(t) &= \tau(t, S(t), I(t), U(t)) - \nu I(t),\; t \geq t_0,\\
R'(t) &= \nu_1 I(t) - \eta R(t),\; t \geq t_0,\\
U'(t) &= \nu_2 I(t) - \eta U(t),\; t \geq t_0,\\
S(t_0) &> 0,\; I(t_0),\; R(t_0),\; U(t_0)\; \geq 0.
\end{aligned} \tag{1}
$$

Stage I: The epidemic exponential stage.

The parameters for Stage I are obtained as follows: A time interval is selected during which the cumulative reported cases appear to be growing exponentially. The exponentially growing curve $CR(t)$ of the cumulative reported cases in the model during Stage I, is estimated according to the formula:

$$CR(t) = a\, e^{b\, t} - c. \tag{2}$$

The positive values a, b, c are fitted to the cumulative reported cases data during this selected time interval, We typically set the value $c = 1$, but allow for other values. The starting time t_0 of Stage I is then given by

$$t_0 = \frac{log(c) \, - \, log(a)}{b}. \tag{3}$$

Parameters and initial values for Stage I

The transmission rate during Stage I is

$$\tau(t, S(t), I(t), U(t)) = \tau_0 \, S(t) \, (I(t) \; + \; U(t)), \tag{4}$$

where

$$\tau_0 = \left(\frac{b \, + \, \nu}{S(t_0)} \right) \left(\frac{b \, + \, \eta}{b \, + \, \eta \, + \, \nu_2} \right). \tag{5}$$

The initial values at time $t_0 = (log(c) \; - \; log(a))/b$ are
$S(t_0) =$ population of the epidemic region,

$$I(t_0) = \frac{b \, c}{f \, \nu}, \;\; U(t_0) = \frac{(1 - f) \, \nu}{b \, + \, \eta} I(t_0), \;\; R(t_0) = 1. \tag{6}$$

The basic reproductive number during Stage I is given by

$$\mathcal{R}_0 = \left(\frac{\tau_0 \, S(t_0)}{\nu} \right) \left(\frac{\eta \, + \, \nu_2}{\eta} \right) = \left(\frac{b + \nu}{\nu} \right) \left(\frac{b \, + \, \eta}{b \, + \, \eta \, + \, \nu_2} \right) \left(\frac{\eta \, + \, \nu_2}{\eta} \right). \tag{7}$$

The transmission rate parameter for Stage II

When major government measures such as social distancing, masks, isolation, quarantine, and public closings are implemented, Stage II begins.

The time dependent transmission rate during Stage II has the form

$$\tau_0 \, S(t) \, (I(t) + U(t)) e^{-\mu(t - t_1)}, \; t_1 \leq t \leq t_2.$$

The transmission rate depends on $I(t)$ (asymptomatic infected individuals) and $U(t)$ (unreported symptomatic infected individuals).

Reported infected individuals $R(t)$ are assumed to be isolated, and do not produce new infections.

The transmission rate parameters for Stage III

When major government measures such as social distancing, masks, isolation, quarantine, and public closings are relaxed, Stage III begins. During Stage III, almost all transmissions arise from asymptomatic infected individuals.

Formulas for the time-dependent transmission rate during Stage III, which begins on day $t_2 > t_1$, for time intervals $[t_n, t_{n+1}]$, $n = 2, 3, \ldots N$, independent of symptomatic infectious cases $U(t)$:

$$\tau(t, S(t), I(t), U(t))) = \alpha_n \tau_0 S(t) I(t), \; t_n \leq t < t_{n+1}, \; n = 2, 3, \ldots N, \quad (8)$$

with $\alpha_n \in (0, 1)$ chosen to fit reported cases data.

The daily reported cases, cumulative reported cases, and cumulative unreported cases from the model

The daily number of reported cases $DR(t)$ at time t in the model is obtained from the solution of the equation

$$DR'(t) = \nu_1 I(t) - DR(t), t \geq t_0, \;\; DR(t_0) = DR_0.$$

The cumulative number of reported cases $CR(t)$ at time t from the model is

$$CR(t) = \nu_1 \int_{t_0}^{t} I(\sigma) d\sigma, t \geq t_0.$$

The cumulative number of unreported cases $CU(t)$ at time t from the model is

$$CU(t) = \nu_2 \int_{t_0}^{t} I(s) ds, t \geq t_0.$$

We illustrate the model for the COVID-19 epidemic in Spain.

We set $\nu = 1/7$ and $f = .4$, which means that asymptomatic infectious individuals remain infectious for 7 days. The fraction f of asymptomatic infectious become reported symptomatic infectious at rate $\nu_1 = f\,\nu$, and the fraction $1 - f$ become unreported symptomatic infectious at rate $\nu_2 = (1 - f)\,\nu$,

We set $\eta = 1/7$, which means that reported symptomatic individuals $R(t)$ are infectious for an average period of $1/\eta = 7$ days, as are unreported symptomatic individuals $U(t)$.

We set the initial susceptible population $S(t_0) = 46,700,000$, the present population of Spain.

Data for the COVID-19 epidemic in Spain

The data for the COVID-19 epidemic in Spain is from Worldometer

https://www.worldometers.info/coronavirus/country/spain.

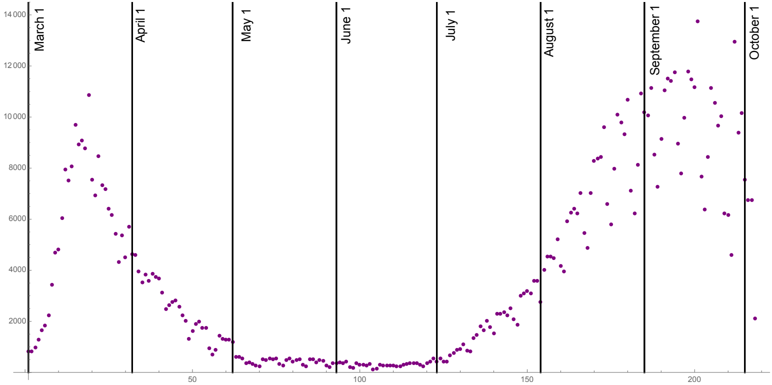


Figure : Daily reported cases from March 1 to October 5.

Cumulative reported cases data for the COVID-19 epidemic in Spain

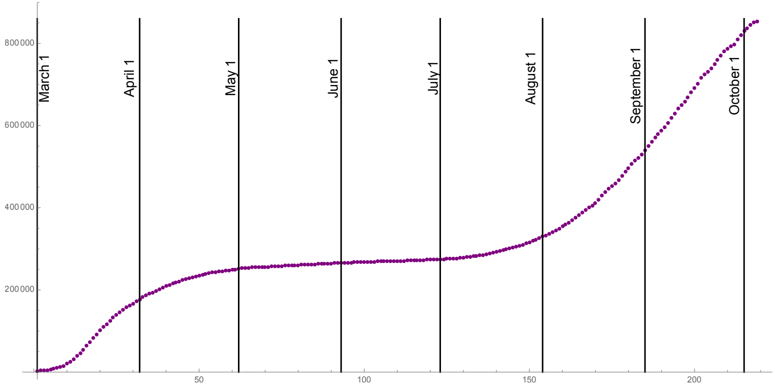


Figure : Cumulative daily reported cases from March 1 to October 5.

The daily reported cases can be smoothed by advancing each day with the average over the preceding week.

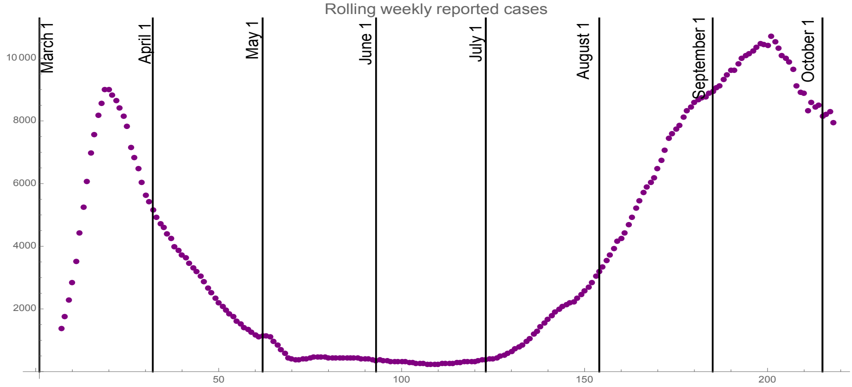


Figure : Rolling weekly averaged number of daily reported cases from March 7 to October 5.

Parameters and initial values for Stage I in Spain

The time interval chosen for exponential growth of reported cases in Stage I is March 4 to March 11. The cumulative cases data on this interval are fitted to the formula $a\,exp(b\,t) - 1$ with the values $a = 2005.0$ and $b = 0.23$. From these values of a and b, the parameters $t_0 = -33.1$, $\tau_0 = 6.49 \times 10^{-9}$, the initial values $I(t_0) = 4.0$, $R(t_0) = 1.0$, $U(t_0) = 0.93$ for Stage I.

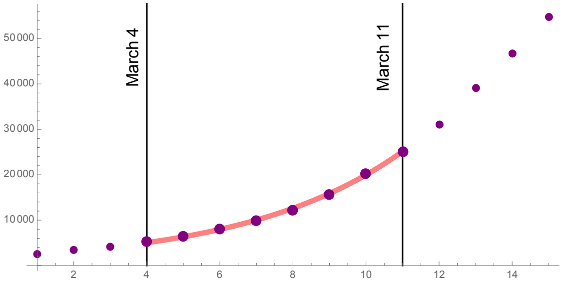


Figure : Dots: cumulative reported cases data from March 1 to March 15. Red graph: $a\,exp(b\,t) - 1$.

The basic reproductive number $\mathcal{R}_0$ of the epidemic in Stage I

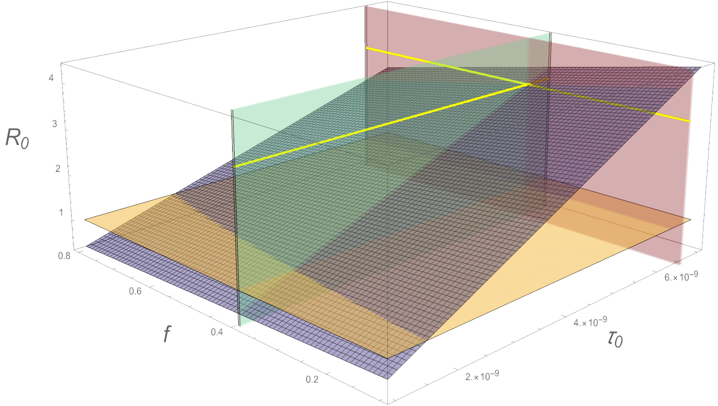


Figure : $\mathcal{R}_0$ as a function of reported cases fraction f and transmission rate τ_0. Baseline values $f = 0.4$, $\tau_0 = 6.49 \times 10^{-9}$, $\mathcal{R}_0 = 3.4$. Orange plane $\equiv 1$.

TheTime Dependent Transmission Rate $\tau_1(t, S, I, U)$ during Stages II and III

The time dependent transmission rate during Stage II is

$$\tau(t, S(t), I(t), U(t))) = \tau_0 \, S(t) \, (I(t) + U(t)) \, e^{-\mu \, (t - t_1)}$$

$t_1 \leq t \leq t_2$, $t_1 = 8$ (March 8), $t_2 = 30$ (March 30), $\mu = 0.09$

(transmission is dependent on symptomatic unreported cases $U(t)$).

The formulas for the time dependent transmission rate during Stage III are

$$\tau(t, S(t), I(t), U(t))) = \alpha_n \tau_0 S(t) I(t), t_n \leq t < t_{n+1}, n = 2, 3, \ldots, 12.$$

(transmission is not dependent on symptomatic unreported cases $U(t)$).

Since $S(t) \approx S(t_n)$ on $[t_n, t_{n+1}]$,

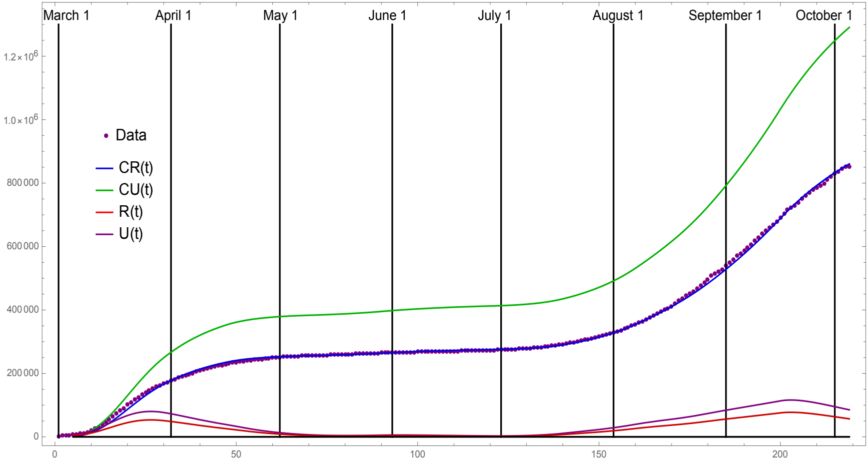
$$I'(t) \approx (\alpha_n \tau_0 S(t_n) - \nu) I(t) \Rightarrow I(t) \approx exp[(\alpha_n \tau_0 S(t_n) - \nu) \, (t - t_n)] I(t_n).$$

The Time Dependent Transmission Rate $\tau_1(t, S, I, U)$

```
τ1[t, S, I, U] = τ0 (I + U) * S,  t ≤ 8.0  Mar 8
τ1[t, S, I, U] = τ0 (I + U) * S * Exp[.09 (t - 8.0)],
8.0 < t ≤ 30.0  Mar 8 - Mar 20
τ1[t, S, I, U] = .30 * τ0 I S,  30 < t ≤ 47  Mar 30 - Apr 16
τ1[t, S, I, U] = .10 * τ0 I S,  47 < t ≤ 55  Apr 16 - Apr 24
τ1[t, S, I, U] = .15 * τ0 I S,  55 < t ≤ 70  Apr 24 - May 9
τ1[t, S, I, U] = .65 * τ0 I S,  70 < t ≤ 90  May 9 - May 29
τ1[t, S, I, U] = .35 * τ0 I S,  90 < t ≤ 120 May 29 - Jun 28
τ1[t, S, I, U] = .85 * τ0 I S,  120 < t ≤ 140 Jun 28 - Jul 18
τ1[t, S, I, U] = .65 * τ0 I S,  140 < t ≤ 160 Jul 18 - Aug 7
τ1[t, S, I, U] = .55 * τ0 I S,  160 < t ≤ 170 Aug 7 - Aug 17
τ1[t, S, I, U] = .59 * τ0 I S,  170 < t ≤ 180 Aug 17 - Aug 27
τ1[t, S, I, U] = .55 * τ0 I S,  180 < t ≤ 200 Aug 27 - Sep 16
τ1[t, S, I, U] = .38 * τ0 I S,  200 < t ≤ 219 Sep 16 - Oct 5
```

Stage I: $t_0 \leq t < 8$; Stage II: $8 \leq t < 30$; Stage III: $30 \leq t \leq 219$.

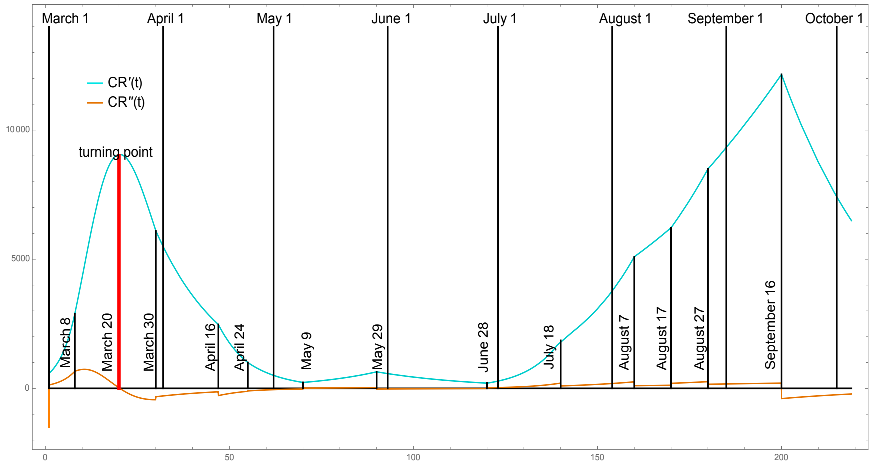
Comparison of the model simulation of daily reported cases to daily reported case data:



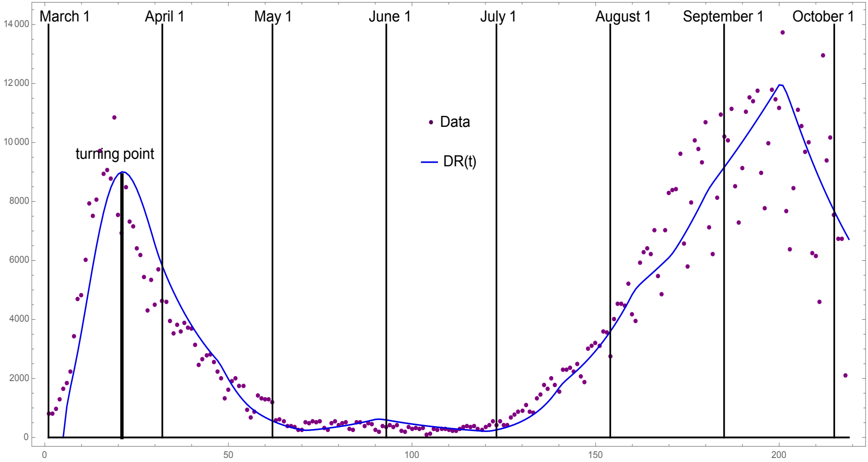
The α_n values specify the concavity of cumulative reported cases $CR(t)$ in the model simulation on $[t_n, t_{n+1}]$. Since $I'(t) \approx \left(\alpha_n\, \tau_0\, S(t_n) - \nu\right) I(t),\ t \in [t_n, t_{n+1}]$, the concavity of $CR(t)$ depends on the sign of $\alpha_n\, \tau_0\, S(t_n) - \nu$:

$$CR(t) = \nu_1 \int_{t_n}^{t} I(s)ds,\ CR'(t) = \nu_1 I(t),\ CR''(t) \approx \nu_1 \left(\alpha_n\, \tau_0\, S(t_n) - \nu\right) I(t).$$

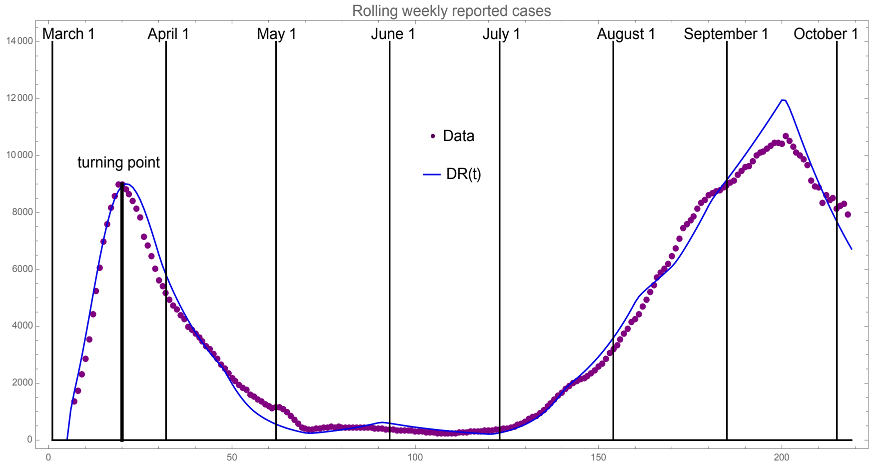
Concave up means worsening epidemic. Concave down means improving epidemic.



Comparison of the model simulation of daily reported cases to daily reported case data:

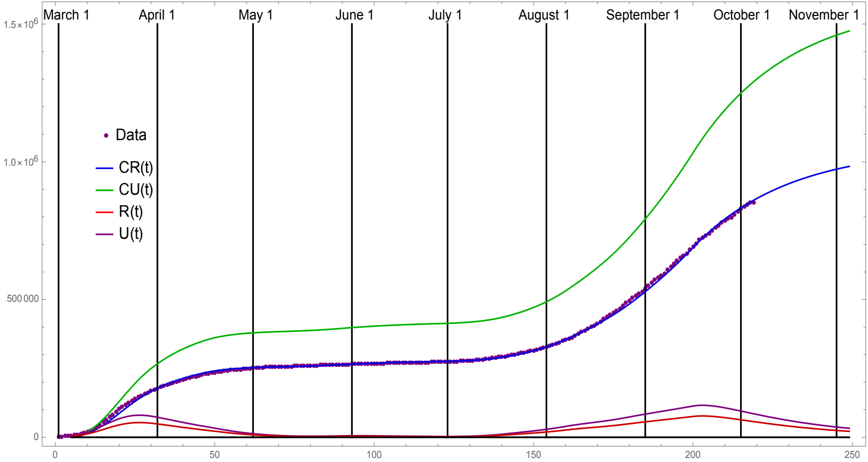


Comparison of the model simulation of daily reported cases to weekly rolling averaged daily reported case data:



Extension of the model simulation from October 5 to November 5

The model simulation of the cumulative number cases increases by approximately 123,000 cases.



Conclusions

1. Our prediction of the evolution of a COVID-19 epidemic is based on three stages in a differential equations model.
2. Stage I is an exponential growth phase before major social distancing measures. Stage II is a diminution of the epidemic due to the implementation of such measures. Stage III is a re-opening of social distancing and a potential second wave of the epidemic.
3. The dynamics of the model include asymptomatic and symptomatic infectiousness, and reported and unreported cases.
4. Application of the model requires identification of parameters specific to a given region based on reported cases data.
5. The example of Spain illustrates Stage III. The development of a second wave depends on the level of social distancing in the re-opening in Stage III.

References

1. (with Z. Liu, P. Magal, and O. Seydi) A COVID-19 epidemic model with latency period, *Infectious Disease Modelling* 5 (2020), 323-337.
2. (with Z. Liu, P. Magal, and O. Seydi) Understanding unreported cases in the 2019-nCov epidemic outbreak in Wuhan, China, and the importance of major public health interventions, *Biology* Vol. 9(3), (2020).
3. (with Z. Liu, P. Magal, and O. Seydi), Predicting the cumulative number of cases for the COVID-19 epidemic in China from early data, *Mathematical Biosciences and Engineering* 17(4) 2020, 3040-3051.
4. (with Z. Liu, P. Magal, and O. Seydi), A model to predict COVID-19 epidemics with applications to South Korea, Italy, and Spain, *SIAM News*, May 2020 issue.
5. (with W.E. Fitzgibbon, J.J.Morgan, and Y. Wu), Analysis of a reaction-diffusion epidemic model with asymptomatic transmission, *J. Biol. Sys.* https://doi.org/10.1142/S0218339020500126.
6. (with Z. Liu and P. Magal), Predicting the number of reported and unreported cases for the COVID-19 epidemic in China, South Korea, Italy, France, Germany and United Kingdom, published online in *J. Theoret. Biol.* (2020).