Short-term predictions and prevention strategies for COVID-2019: A model based study

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Abstract

An outbreak of respiratory disease caused by a novel coronavirus is ongoing till December 2019. As of March 16 2020, It has caused an epidemic outbreak with more than 1,79,073 confirmed infections and 7,074 reported deaths worldwide. During the period of an epidemic when human-to-human transmission is established and reported cases of coronavirus disease (COVID) are rising worldwide, forecasting is of utmost importance for health care planning and control the virus with limited resource. In this study, we propose and analyze a compartmental epidemic model of COVID to predict and control the outbreak. The basic reproduction number and control reproduction number are calculated analytically. A detailed stability analysis of the model is performed to observe the dynamics of the system. We calibrated the proposed model to fit daily data from five provinces of China namely, Hubei, Guangdong, Henan, Zhejiang and Hunan. Our findings suggest that independent self-sustaining human-to-human spread ($R_0 > 1$, $R_c > 1$) is already present in all the five provinces. Short-term predictions show that the decreasing trend of new COVID cases is well captured by the model for all the five provinces. However, long term predictions for Hubei reveals that the symptomatic COVID cases will show oscillatory behaviour. Futher, we found that effective management of quarantined individuals is more effective than management of isolated individuals to reduce the disease burden. Numerical results show that the modification factor for quarantine, modification factor for isolation and transmission rate are quite effective in reduction of the COVID cases in Hubei. Thus, COVID is controllable by reducing contacts with infected people and increasing the efficiency of quarantine and isolation. Health care officials should supply medications, protective masks and necessary human resources in the affected areas.

Keywords: Coronavirus disease, Mathematical model, Basic reproduction number, Model calibration, Prediction, Control strategies, China.

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1. Introduction

In December 2019, an outbreak of novel coronavirus (2019-nCoV) infected with viral pneumonia infection [30; 53], which is lethal, was first noted in Wuhan, the sprawling capital of the Hubei province of Central China [1] declared by the Health Commission of Hubei Province. Now coronavirus is officially called COVID-19 by WHO (World Health Organization). The outbreak was declared a Public Health Emergency of International Concern on 30 January 2020 by WHO. Coronaviruses are enveloped positive-sense, non-segmented RNA viruses belonging to the Coronaviridae family and the Nidovirales order and widely distributed in humans and other mammals [30]. The virus is responsible for a range of symptoms including dry cough, fever, fatigue, breathing difficulty, and bilateral lung infiltration in severe cases, similar to those caused by SARS-CoV and MERS-CoV infections[30; 26]. Many people may experience non-breathing symptoms including nausea, vomiting and diarrhea [4]. Some patients have reported radiographic changes in their ground-glass lungs; normal or lower than average white blood cell lymphocyte, and platelet counts; hypoxaemia; and deranged liver and renal function. Most of them were said to be geographically connected to the Huanan seafood wholesale market, which was subsequently claimed by journalists to be selling freshly slaughtered game animals [3]. The Chinese health authority said the patients initially tested negative for common respiratory viruses and bacteria but subsequently tested positive for a novel coronavirus (nCoV) [15]. In contrast to the initial findings [17], the 2019-nCoV virus spreads from person to person as confirmed in [15]. It has become an epidemic outbreak with more than 1,79,073 confirmed infections and 7,074 reported deaths worldwide as of 16 March 2020. The current epidemic outbreak had resulted in 81,048 (67794 of which are in Hubei) confirmed cases and 3204 (3085 of which were in Hubei) deaths in China [1; 6], and sporadic cases exported from Wuhan have been reported in Thailand, Japan, Republic of Korea, Hong Kong, Taiwan, Australia, Italy and the United States and have spread to 155 countries so far [6; 1]. Since first discovery and identification of coronavirus in 1965, three major outbreaks occurred, caused by emerging, highly pathogenic coronaviruses, namely the 2003 outbreak of Severe Acute Respiratory Syndrome (SARS) in mainland China [27; 36], the 2012 outbreak of Middle East Respiratory Syndrome (MERS) in Saudi Arabia [21; 22], and the 2015 outbreak of MERS in South Korea [20; 33]. These outbreaks resulted in SARS and MERS cases confirmed by more than 8000 and 2200, respectively [34]. The COVID-19 is caused by a new genetically similar corona virus to the viruses that cause SARS and MERS. Despite a relatively lower death rate compared to SARS and MERS, the COVID-19 spreads rapidly and infects more people than the SARS and MERS outbreaks. In spite of strict intervention measures implemented in the region where the infection originated, the infection spread locally in Wuhan, in China and around the globally.

Though COVID-19 laboratory testing ramped up rapidly in China and elsewhere as of January 2020, China's central government and all local governments, including Hubei, have tightened preventive measures to reduce the spread of COVID-19. Many major cities in Hubei province were locked up and several steps were taken, such as quarantining infected cases, tracing close contacts, promoting social consensus on self-protection such as wearing face masks in public places, etc. To control the outbreak, Chinese government actively restricts the movement of more than 50 million people in Central China, which is considered one of the largest quarantine in human history. More than 42,600 people have been diagnosed with coronavirus in China as of February 10 [1]. The country is literally at a standstill and the disease has seriously impacted the economy and the livelihood of the people.

As the 2019 coronavirus disease outbreak (COVID-19) is expanding rapidly in China and beyond, with the potential for becoming a global pandemic [2], real-time analyzes of epidemiological data are required to increase situational awareness and inform interventions [43]. Earlier, in the first few weeks of an outbreak, real-time analyzes shed light on the severity, transmissibility, and natural history of an emerging pathogen, such as SARS, the 2009 influenza pandemic, and Ebola [18; 19; 24; 37]. Analysis of detailed patient line lists is especially useful for inferring key epidemiological parameters, such as infectious and incubation periods, and delays between infection and detection, isolation and case reporting [18; 19]. However, official patient's health data seldom become available to the public early in an outbreak, when the information is most required. In addition to medical and biological research, theoretical studies based on either mathematical or statistical modeling may also play an important role throughout this anti-epidemic fight in understanding the epidemic character traits of the outbreak, in predicting the inflection point and end time, and in having to decide on the measures to reduce the spread. To this end, many efforts have been made at the early stage to estimate key epidemic parameters, such as the basic reproduction number, serial interval, and doubling time, in which the statistical models are mostly used [40; 35]. An Imperial College London study group calculated that 4000 (95% CI: 1000-9700) cases had occurred in Wuhan with symptoms beginning on January 18, 2020, and an estimated basic reproduction number was 2.6 (95% CI: 1.5-3.5) using the number of cases transported from Wuhan to other countries [32]. Leung et al. reached a similar finding, calculating the number of cases transported from Wuhan to other major cities in China [9] and also suggesting the possibility for the spreading of risk [12] for travel-related diseases. Mathematical modeling based on dynamic equations [25; 45] may provide detailed mechanism for the disease dynamics. A variety of modeling experiments for the COVID-19 outbreak have already been carried out. Wu et al. [49] developed an susceptible exposed infectious recovered model (SEIR) model to explain the dynamics of transmission and predicted national and global disease

spread based on data recorded from 31 December 2019 to 28 January 2020. Tang et al. [46] suggested a compartmental deterministic model incorporating the disease's clinical development, the patient epidemiological status and the intervention steps. They found that the control reproduction number may be as high as 6.47, and that intervention strategies including intense contact tracing accompanied by quarantine and isolation can effectively reduce COVID cases. Using the hypothesis of Poisson-distributed daily time increments Read et al. [41] stated a value of basic reproduction number to be 3.1 based on A SEIR model fitted to real data. Imai et al. [31] performed computational modeling of possible epidemic trajectories in order to estimate the size of the outbreak of the disease in Wuhan, with a emphasis on human to human transmission. Their findings suggest that control measures need to block well over 60% of transmission in order to contain the outbreak effectively. Among these, the classical SEIR is the most widely accepted model for characterizing the COVID outbreak epidemic in China. Since the dynamical model can reach comprehensible conclusions about the outbreak, a cascade of SEIR models is being developed to visualize the mechanisms of transmission from source of infection, hosts, reservoir to human [16].

Using similar modelling framework we aim to predict new COVID cases in five endemic provinces of China. By mathematical analysis of the proposed model we would like to explore transmission dynamics of the virus among humans. Another goal is to study the control strategies that can significantly reduce the outbreak in near future.

2. Model formulation

General mathematical models for the spread of infectious diseases have been described previously [39; 23; 29]. A compartmental differential equation model for COVID is formulated and analyzed. We adopt a variant that reflects some key epidemiological properties of COVID. The model monitors the dynamics of seven sub-populations, namely susceptible ($S(t)$), exposed ($E(t)$), quarantined ($Q(t)$), asymptomatic ($A(t)$), symptomatic ($I(t)$), isolated ($J(t)$) and recovered ($R(t)$) individuals. The total population size is $N(t) = S(t) + E(t) + Q(t) + A(t) + I(t) + J(t) + R(t)$. In this model, quarantine refers to the separation of COVID infected individuals from the general population when the population are infected but not infectious, whereas isolation describes the separation of COVID infected individuals when the population become symptomatic infectious. Our model incorporates some demographic effects by assuming a proportional natural death rate $\mu > 0$ in each of the seven sub-populations of the model. In addition, our model includes a net inflow of susceptible individuals into the region at a rate Π per unit time. This parameter includes new births, immigration and emigration. The flow diagram of the proposed model is displayed in Figure 1.

Susceptible population (S(t)):

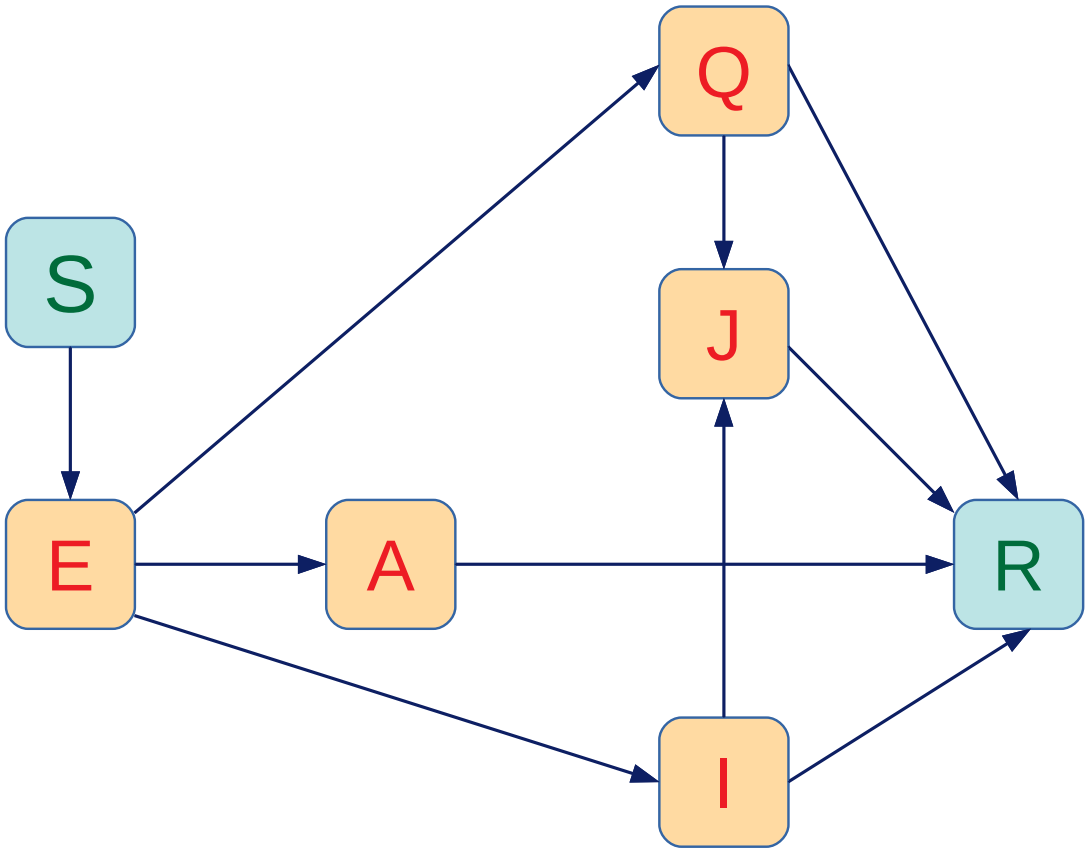

Figure 1: Compartmental flow diagram of the proposed model.

By recruiting individuals into the region, the susceptible population is increased and reduced by natural death. Also the susceptible population decreases after infection, acquired through interaction between a susceptible individual and an infected person who may be quarantined, asymptomatic, symptomatic, or isolated. For these four groups of infected individuals, the transmission coefficients are β, $r_Q\beta$, $r_A\beta$, and $r_J\beta$ respectively. We consider the β as a transmission rate along with the modification factors for quarantined r_Q, asymptomatic r_A and isolated r_J individuals. The interaction between infected individuals (quarantined, asymptomatic, symptomatic or isolated) and susceptible is modelled in the form of total population without quarantined and isolated individuals using standard mixing incidence incidence [38; 39; 23; 29]. The rate of change of the susceptible population can be expressed by the following equation:

$$\frac{dS}{dt} = \Pi - \frac{S(\beta I + r_Q\beta Q + r_A\beta A + r_J\beta J)}{N - Q - J} - \mu S, \tag{2.1}$$

Exposed population(E(t)):

Population who are exposed are infected individuals but not infectious for the community. The exposed population decreases with quarantine at a rate of γ_1, and become asymptomatic and symptomatic at a rate k_1 and natural death at a rate μ. Hence,

$$\frac{dE}{dt} = \frac{S(\beta I + r_Q \beta Q + r_A \beta A + r_J \beta J)}{N - Q - J} - (\gamma_1 + k_1 + \mu)E \tag{2.2}$$

Quarantine population (Q(t)):

These are exposed individuals who are quarantined at a rate γ_1. For convenience, we consider that all quarantined individuals are exposed who will begin to develop symptoms and then transfer to the isolated class. Assuming that a certain portion of uninfected individuals are also quarantined would be more plausible, but this would drastically complicate the model and require the introduction of many parameters and compartments. In addition, the error caused by our simplification is to leave certain people in the susceptible population who are currently in quarantine and therefore make less contacts. The population is reduced by growth of clinical symptom at a rate of k_2 and transferred to the isolated class. σ_1 is the recovery rate of quarantine individuals and μ is the natural death rate of human population. Thus,

$$\frac{dQ}{dt} = \gamma_1 E - (k_2 + \sigma_1 + \mu)Q \tag{2.3}$$

Asymptomatic population(A(t)):

Asymptomatic individuals were exposed to the virus but clinical signs of COVID have not yet developed. The exposed individuals become asymptomatic at a rate k_1 by a proportion p. The recovery rate of asymptomatic individuals is σ_2 and the natural death rate is μ. Thus,

$$\frac{dA}{dt} = pk_1 E - (\sigma_2 + \mu)A \tag{2.4}$$

Symptomatic population(I(t)):

The symptomatic individuals are produced by a proportion of $(1 - p)$ of exposed class after the exposer of clinical symptoms of COVID by exposed individuals. γ_2 is the isolation rate of the symptomatic individuals, σ_3 is the recovery rate and natural death at a rate μ. Thus,

$$\frac{dI}{dt} = (1 - p)k_1 E - (\gamma_2 + \sigma_3 + \mu)I \tag{2.5}$$

Isolated population(J(t)):

The isolated individuals are those who have been developed by clinical symptoms and been isolated at hospital. The isolated individuals are come from quarantined community

at a rate k_2 and symptomatic group at a rate γ_2. The recovery rate of isolated individuals is σ_4, disease induced death rate is δ and natural death rate is μ. Thus,

$$\frac{dJ}{dt} = k_2 Q + \gamma_2 I - (\delta + \sigma_4 + \mu)J \tag{2.6}$$

Recovered population(R(t)):

Quarantined, asymptomatic, symptomatic and isolated individuals recover from the disease at rates σ_1, σ_2, σ_3 and σ_4; respectively, and this population is reduced by a natural death rate μ. Thus,

$$\frac{dR}{dt} = \sigma_1 Q + \sigma_2 A + \sigma_3 I + \sigma_4 J - \mu R \tag{2.7}$$

From the above considerations, the following system of ordinary differential equations governs the dynamics of the system:

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \frac{S(\beta I + r_Q \beta Q + r_A \beta A + r_J \beta J)}{N - Q - J} - \mu S, \\
\frac{dE}{dt} &= \frac{S(\beta I + r_Q \beta Q + r_A \beta A + r_J \beta J)}{N - Q - J} - (\gamma_1 + k_1 + \mu)E, \\
\frac{dQ}{dt} &= \gamma_1 E - (k_2 + \sigma_1 + \mu)Q, \\
\frac{dA}{dt} &= p k_1 E - (\sigma_2 + \mu)A, \\
\frac{dI}{dt} &= (1-p) k_1 E - (\gamma_2 + \sigma_3 + \mu)I, \\
\frac{dJ}{dt} &= k_2 Q + \gamma_2 I - (\delta + \sigma_4 + \mu)J, \\
\frac{dR}{dt} &= \sigma_1 Q + \sigma_2 A + \sigma_3 I + \sigma_4 J - \mu R,
\end{aligned} \tag{2.8}$$

All the parameters and their biological interpretation are given in Table 1 respectively.

Table 1: Description of parameters used in the model.

Parameters	Interpretation	Value	Reference
Π	Recruitement rate	-	[10]
β	Transmission rate	-	Estimated
r_Q	Modification factor for quarantined	0.3	Assumed
r_A	Modification factor for asymptomatic	0.45	Assumed
r_J	Modification factor for isolated	0.6	Assumed
γ_1	Rate at which the exposed individuals are diminished by quaratine	-	Estimated
γ_2	Rate at which the symptomatic individuals are diminished by isolation	-	Estimated
k_1	Rate at which exposed become infected	1/7	[1]
k_2	Rate at which quaratined individuals are isolated	-	Estmated
p	Proportion of asymptomatic individuals	0.13166	[46]
σ_1	Recovery rate from quarantined individuals	-	Estimated
σ_2	Recovery rate from asymptomatic individuals	-	Estimated
σ_3	Recovery rate from symptomatic individuals	0.46	[1]
σ_4	Recovery rate from isolated individuals	-	Estimated
δ	Diseases induced mortality rate	-	Data
μ	Natural death rate	0.3589×10^{-4}	[8]

3. Mathematical analysis

3.1. ***Positivity and boundedness of the solution***

This subsection is provided to prove the positivity and boundedness of solutions of the system (2.8) with initial conditions $(S(0), E(0), Q(0), A(0), I(0), J(0), R(0))^T \in R^7_+$. We first state the following lemma.

Lemma 3.1. *Suppose* $\Omega \subset \mathbb{R}\times\mathbb{C}^n$ *is open,* $f_i \in C(\Omega, \mathbb{R}), i = 1, 2, 3, ..., n$. *If* $f_i|_{x_i(t)=0, X_t\in\mathbb{C}^n_{+0}} \geq 0$, $X_t = (x_{1t}, x_{2t}, ..., x_{1n})^T, i = 1, 2, 3, ..., n$, *then* $\mathbb{C}^n_{+0}\{\phi = (\phi_1, ..., \phi_n) : \phi \in \mathbb{C}([-\tau, 0], \mathbb{R}^n_{+0})\}$ *is the invariant domain of the following equations*

$$\frac{dx_i(t)}{dt} = f_i(t, X_t), t \geq \sigma, i = 1, 2, 3, ..., n.$$

where $\mathbb{R}^n_{+0} = \{(x_1, ...x_n) : x_i \geq 0, i = 1, ..., n\}$ *[50].*

Proposition 3.1. *The system* (2.8) *is invariant in* $\mathbb{R}^7_+$.

Proof. By re-writing the system (2.8) we have

$$\frac{dX}{dt} = M(X(t)), X(0) = X_0 \geq 0 \tag{3.1}$$

$M(X(t)) = (M_1(X), M_1(X), ..., M_7(X))^T$
We note that

$$\begin{aligned}
\frac{dS}{dt}|_{S=0} &= \Pi \geq 0,\\
\frac{dE}{dt}|_{E=0} &= \frac{S(\beta I + r_Q\beta Q + r_A\beta A + r_J\beta J)}{S + A + I + R} \geq 0,\\
\frac{dQ}{dt}|_{Q=0} &= \gamma_1 E \geq 0,\\
\frac{dA}{dt}|_{A=0} &= pk_1 E \geq 0,\\
\frac{dI}{dt}|_{I=0} &= (1-p)k_1 E \geq 0,\\
\frac{dJ}{dt}|_{J=0} &= k_2 Q + \gamma_2 I \geq 0,\\
\frac{dR}{dt}|_{R=0} &= \sigma_1 Q + \sigma_2 A + \sigma_3 I + \sigma_4 J \geq 0.
\end{aligned}$$

Then it follows from the Lemma 3.1 that $\mathbb{R}^7_+$ is an invariant set. □

Proposition 3.2. *The system* (2.8) *is bounded in the region*
$\Omega = \{(S + E + Q + A + I + J + R \in \mathbb{R}^7_+ | S + E + Q + A + I + J + R \leq \frac{\Pi}{\mu}\}$

Proof. We observed from the system that

$$\begin{aligned}
&\frac{dN}{dt} = \Pi - \mu N - \delta J \leq \Pi - \mu N\\
&\Longrightarrow \lim_{t\to\infty} supN(t) \leq \frac{\Pi}{\mu}
\end{aligned}$$

Hence the system (2.8) is bounded. □

3.2. ***Diseases-free equilibrium and control reproduction number***

The diseases-free equilibrium can be obtained for the system (2.8) by putting $E = 0, Q = 0, A = 0, I = 0, J = 0$, which is denoted by $P_1^0 = (S^0, 0, 0, 0, 0, 0, R^0)$, where

$$S^0 = \frac{\Pi}{\mu}, R^0 = 0.$$

The control reproduction number, a central concept in the study of the spread of communicable diseases, is e the number of secondary infections caused by a single infective

in a population consisting essentially only of susceptibles with the control measures in place (quarantined and isolated class) [47]. This dimensionless number is calculated at the DFE by next generation operator method [48; 23] and it is denoted by R_c.

For this, we assemble the compartments which are infected from the system (2.8) and decomposing the right hand side as $\mathcal{F} - \mathcal{V}$, where $\mathcal{F}$ is the transmission part, expressing the the production of new infection, and the transition part is $\mathcal{V}$, which describe the change in state.

$$\mathcal{F} = \begin{bmatrix} \frac{S(\beta I + r_Q \beta Q + r_A \beta A + r_J \beta J)}{N-Q-J} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \mathcal{V} = \begin{bmatrix} (\gamma_1 + k_1 + \mu)E \\ -\gamma_1 E + (k_2 + \sigma_1 + \mu)Q \\ -pk_1 E + (\sigma_2 + \mu)A \\ -(1-p)k_1 E + (\gamma_2 + \sigma_3 + \mu)I \\ -k_2 Q - \gamma_2 I + (\delta + \sigma_4 + \mu)J \end{bmatrix}$$

Now we calculate the jacobian of $\mathcal{F}$ and $\mathcal{V}$ at DFE P_1^0

$$F = \frac{\partial \mathcal{F}}{\partial X} = \begin{bmatrix} 0 & r_Q\beta & r_A\beta & \beta & r_J\beta \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

$$V = \frac{\partial \mathcal{V}}{\partial X} = \begin{bmatrix} \gamma_1 + k_1 + \mu & 0 & 0 & 0 & 0 \\ -\gamma_1 & k_2 + \sigma_1 + \mu & 0 & 0 & 0 \\ -pk_1 & 0 & \sigma_2 + \mu & 0 & 0 \\ -(1-p)k_1 & 0 & 0 & \gamma_2 + \sigma_3 + \mu & 0 \\ 0 & -k_2 & 0 & -\gamma_2 & \delta + \sigma_4 + \mu \end{bmatrix}.$$

Following [28], $R_c = \rho(FV^{-1})$, where ρ is the spectral radius of the next-generation matrix (FV^{-1}). Thus, from the model (2.8), we have the following expression for R_c and R_0:

$$\begin{aligned} R_c = {} & \frac{r_Q \beta \gamma_1}{(\gamma_1 + k_1 + \mu)(k_2 + \sigma_1 + \mu)} + \frac{r_A \beta p k_1}{(\gamma_1 + k_1 + \mu)(\sigma_2 + \mu)} \\ & + \frac{\beta k_1 (1-p)}{(\gamma_1 + k_1 + \mu)(\gamma_2 + \sigma_3 + \mu)} + \frac{r_J \beta \gamma_1 k_2}{(\gamma_1 + k_1 + \mu)(k_2 + \sigma_1 + \mu)(\delta + \sigma_4 + \mu)} \\ & + \frac{r_J \beta (1-p) k_1 \gamma_2}{(\gamma_1 + k_1 + \mu)(\gamma_2 + \sigma_3 + \mu)(\delta + \sigma_4 + \mu)} \end{aligned} \tag{3.2}$$

3.3. ***Stability of DFE***

Theorem 3.1. *The diseases free equilibrium(DFE)* $P_1^0 = (S^0, 0, 0, 0, 0, 0, R^0)$ *of the system* (2.8) *is locally asymptotically stable if* $R_c < 1$ *and unstable if* $R_c > 1$.

Proof. We calculate the Jacobian of the system (2.8) at DFE, and is given by

$$J_{P_1^0} = \begin{bmatrix} -\mu & 0 & -r_Q\beta & -r_A\beta & -\beta & -r_J\beta & 0 \\ 0 & -(\gamma_1+k_1+\mu) & r_Q\beta & r_A\beta & \beta & r_J\beta & 0 \\ 0 & \gamma_1 & -(k_2+\sigma_1+\mu) & 0 & 0 & 0 & 0 \\ 0 & pk_1 & 0 & -(\sigma_2+\mu) & 0 & 0 & 0 \\ 0 & (1-p)k_1 & 0 & 0 & -(\gamma_2+\sigma_3+\mu) & 0 & 0 \\ 0 & 0 & k_2 & 0 & \gamma_2 & -(\delta+\sigma_4+\mu) & 0 \\ 0 & 0 & \sigma_1 & \sigma_2 & \sigma_3 & \sigma_4 & -\mu \end{bmatrix},$$

Let λ be the eigenvalue of the matrix $J_{P_1^0}$. Then the characteristic equation is given by $det(J_{P_1^0} - \lambda I) = 0$.
$\Rightarrow r_J\beta\gamma_1k_2(\lambda+\sigma_2+\mu)(\lambda+\gamma_2+\sigma_3+\mu) + r_J\beta\gamma_2k_1(\lambda+k_2+\sigma_1+\mu)[(1-p)(\lambda+\sigma_2+\mu)] + r_A\beta pk_1(\lambda+\gamma_2+\sigma_3+\mu)(\lambda+\delta+\sigma_4+\mu)(\lambda+k_2+\sigma_1+\mu) + \beta k_1[(1-p)(\lambda+\sigma_2+\mu)](\lambda+\delta+\sigma_4+\mu)(\lambda+k_2+\sigma_1+\mu) - (\lambda+\gamma_1+k_1+\mu)(\lambda+\sigma_2+\mu)(\lambda+\gamma_2+\sigma_3+\mu)(\lambda+\delta+\sigma_4+\mu)(\lambda+k_2+\sigma_1+\mu) = 0.$
Which can be written as

$$\frac{r_Q\beta\gamma_1}{(\lambda+\gamma_1+k_1+\mu)(\lambda+k_2+\sigma_1+\mu)} + \frac{r_A\beta pk_1}{(\lambda+\gamma_1+k_1+\mu)(\lambda+\sigma_2+\mu)} + \frac{\beta k_1(1-p)}{(\lambda+\gamma_1+k_1+\mu)(\lambda+\gamma_2+\sigma_3+\mu)} + \frac{r_J\beta[\gamma_1k_2(\lambda+\sigma_2+\mu)(\lambda+\gamma_2+\sigma_3+\mu) + (1-p)k_1\gamma_2(\lambda+k_2+\sigma_1+\mu)(\lambda+\sigma_2+\mu)]}{(\lambda+\gamma_1+k_1+\mu)(\lambda+k_2+\sigma_1+\mu)(\lambda+\sigma_2+\mu)(\lambda+\gamma_2+\sigma_3+\mu)(\lambda+\delta+\sigma_4+\mu)} = 1.$$

Denote

$$\begin{aligned} G_1(\lambda) = {} & \frac{r_Q\beta\gamma_1}{(\lambda+\gamma_1+k_1+\mu)(\lambda+k_2+\sigma_1+\mu)} + \frac{r_A\beta pk_1}{(\lambda+\gamma_1+k_1+\mu)(\lambda+\sigma_2+\mu)} \\ & + \frac{\beta k_1(1-p)}{(\lambda+\gamma_1+k_1+\mu)(\lambda+\gamma_2+\sigma_3+\mu)} \\ & + \frac{r_J\beta\gamma_1k_2}{(\lambda+\gamma_1+k_1+\mu)(\lambda+k_2+\sigma_1+\mu)(\lambda+\delta+\sigma_4+\mu)} \\ & + \frac{r_J\beta(1-p)k_1\gamma_2}{(\lambda+\gamma_1+k_1+\mu)(\lambda+\gamma_2+\sigma_3+\mu)(\lambda+\delta+\sigma_4+\mu)}. \end{aligned}$$

We rewrite $G_1(\lambda)$ as $G_1(\lambda) = G_{11}(\lambda) + G_{12}(\lambda) + G_{13}(\lambda) + G_{14}(\lambda) + G_{15}(\lambda)$

Now if $Re(\lambda) \geq 0$, $\lambda = x + iy$, then

$$|G_{11}(\lambda)| \leq \frac{r_Q \beta \gamma_1}{|\lambda + \gamma_1 + k_1 + \mu||\lambda + k_2 + \sigma_1 + \mu|} \leq G_{11}(x) \leq G_{11}(0)$$
$$|G_{12}(\lambda)| \leq \frac{r_A \beta p k_1}{|\lambda + \gamma_1 + k_1 + \mu||\lambda + \sigma_2 + \mu|} \leq G_{12}(x) \leq G_{12}(0)$$
$$|G_{13}(\lambda)| \leq \frac{\beta k_1 (1-p)}{|\lambda + \gamma_1 + k_1 + \mu||\lambda + \gamma_2 + \sigma_3 + \mu|} \leq G_{13}(x) \leq G_{13}(0)$$
$$|G_{14}(\lambda)| \leq \frac{r_J \beta \gamma_1 k_2}{|\lambda + \gamma_1 + k_1 + \mu||\lambda + k_2 + \sigma_1 + \mu||\lambda + \delta + \sigma_4 + \mu|} \leq G_{14}(x) \leq G_{14}(0)$$
$$|G_{15}(\lambda)| \leq \frac{r_J \beta (1-p) k_1 \gamma_2}{|\lambda + \gamma_1 + k_1 + \mu||\lambda + \gamma_2 + \sigma_3 + \mu||\lambda + \delta + \sigma_4 + \mu|} \leq G_{15}(x) \leq G_{15}(0)$$

Then $G_{11}(0) + G_{12}(0) + G_{13}(0) + G_{14}(0) + G_{15}(0) = G_1(0) = R_c < 1$, which implies $|G_1(\lambda)| \leq 1$.
Thus for $R_c < 1$, all the eigenvalues of the characteristics equation $G_1(\lambda) = 1$ has negative real parts.

Therefore if $R_c < 1$, all eigenvalues are negative and hence DFE P_1^0 is locally asymptotically stable.

Now if we consider $R_c > 1$ i.e $G_1(0) > 1$, then

$$\lim_{\lambda \to \infty} G_1(\lambda) = 0.$$

Then there exist $\lambda_1^* > 0$ such that $G_1(\lambda_1^*) = 1$.

That means there exist positive eigenvalue $\lambda_1^* > 0$ of the Jacobian matrix.

Hence DFE P_1^0 is unstable whenever $R_c > 1$. □

Theorem 3.2. *The diseases free equilibrium (DFE) $P_1^0 = (S^0, 0, 0, 0, 0, 0, R^0)$ is globally asymptotically stable (GAS) for the system (2.8) if $R_c < 1$ and unstable if $R_c > 1$.*

Proof. We rewrite the system (2.8) as

$$\frac{dX}{dt} = F(X, V)$$
$$\frac{dV}{dt} = G(X, V), G(X, 0) = 0$$

where $X = (S, R) \in R_2$ (the number of uninfected individuals compartments), $V = (E, Q, A, I, J) \in R_5$ (the number of infected individuals compartments), and $P_1^0 = (\frac{\Pi}{\mu}, 0, 0, 0, 0, 0, 0)$ is the DFE of the system (2.8). The global stability of the DFE is guaranteed if the following two conditions are satisfied:

1. For $\frac{dX}{dt} = F(X, 0)$, X^* is globally asymptotically stable,
2. $G(X, V) = BV - \widehat{G}(X, V)$, $\widehat{G}(X, V) \geq 0$ for $(X, V) \in \Omega$,

where $B = D_V G(X^*, 0)$ is a Metzler matrix and Ω is the positively invariant set with respect to the model (2.8). Following Castillo-Chavez et al [13], we check for aforementioned conditions.
For system (2.8),

$$F(X,0) = \begin{bmatrix} \Pi - \mu S \\ 0 \end{bmatrix},$$

$$B = \begin{bmatrix} -(\gamma_1 + k_1 + \mu) & r_Q\beta & r_A\beta & \beta & r_J\beta \\ \gamma_1 & -(k_2 + \sigma_1 + \mu) & 0 & 0 & 0 \\ pk_1 & 0 & -(\sigma_2 + \mu) & 0 & 0 \\ (1-p)k_1 & 0 & 0 & -(\gamma_2 + \sigma_3 + \mu) & 0 \\ 0 & k_2 & 0 & \gamma_2 & -(\delta + \sigma_4 + \mu) \end{bmatrix}$$

and

$$\widehat{G}(X,V) = \begin{bmatrix} r_Q\beta Q(1 - \frac{S}{N-Q-J}) + r_A\beta A(1 - \frac{S}{N-Q-J}) + \beta I(1 - \frac{S}{N-Q-J}) + r_J\beta J(1 - \frac{S}{N-Q-J}) \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}.$$

Clearly, $\widehat{G}(X,V) \geq 0$ whenever the state variables are inside Ω. Also it is clear that $X^* = (\frac{\Pi}{d}, 0)$ is a globally asymptotically stable equilibrium of the system $\frac{dX}{dt} = F(X,0)$. Hence, the theorem follows. □

3.4. ***Existence and local stability of endemic equilibrium***

In this section, the existence of the endemic equilibrium of the model (2.8) is established. Let us denote

$$m_1 = \gamma_1 + k_1 + \mu, m_2 = k_2 + \sigma_1 + \mu, m_3 = \sigma_2 + \mu,$$
$$m_4 = \gamma_2 + \sigma_3 + \mu, m_5 = \delta + \sigma_4 + \mu.$$

Let $P^* = (S^*, E^*, Q^*, A^*, I^*, J^*, R^*)$ represents any arbitrary endemic equilibrium point (EEP) of the model (2.8). Further, define

$$\eta^* = \frac{\beta(I^* + r_Q Q^* + r_A A^* + r_J J^*)}{N^* - Q^* - J^*} \tag{3.3}$$

It follows, by solving the equations in (2.8) at steady-state, that

$$S^* = \frac{\Pi}{\eta^* + \mu}, E^* = \frac{\eta^* S^*}{m_1}, Q^* = \frac{\gamma_1 \eta^* S^*}{m_1 m_2}, A^* = \frac{pk_1 \eta^* S^*}{m_1 m_3}, \tag{3.4}$$
$$I^* = \frac{(1-p)k_1 \eta^* S^*}{m_1 m_4}, J^* = \frac{\eta^* S^*(k_2\gamma_1 m_4 + (1-p)k_1\gamma_2 m_2)}{m_1 m_2 m_4 m_5}$$
$$R^* = \frac{\eta^* S^*[\sigma_1\gamma_1 m_3 m_4 m_5 + pk_1\sigma_2 m_2 m_4 m_5 + (1-p)k_1\sigma_3 m_2 m_3 m_5 + m_3\sigma_4(k_2\gamma_1 m_4 + (1-p)k_1\gamma_2 m_2)]}{\mu m_1 m_2 m_3 m_4 m_5}$$

Substituting the expression in (3.4) into (3.3) shows that the non-zero equilibrium of the model (2.8) satisfy the following linear equation, in terms of η^*:

$$A\eta^* + B = 0 \tag{3.5}$$

where

$$\begin{aligned} A &= \mu[m_2m_3m_4m_5 + pk_1m_2m_4m_5 + (1-p)k_1m_2m_3m_5] + \sigma_1\gamma_1m_3m_4m_5 \\ &\quad + \sigma_2pk_1m_2m_4m_5 + (1-p)k_1\sigma_3m_2m_3m_5 + \sigma_4k_2\gamma_1m_3m_4 + (1-p)\sigma_4\gamma_2k_1m_2m_3 \\ B &= \mu m_1m_2m_3m_4m_5(1-R_c) \end{aligned}$$

Since $A > 0$, $\mu > 0$, $m_1 > 0$, $m_2 > 0$, $m_3 > 0$, $m_4 > 0$ and $m_5 > 0$, it is clear that the model (2.8) has a unique endemic equilibrium point (EEP) whenever $R_c > 1$ and no positive endemic equilibrium point whenever $R_c < 1$. This rules out the possibility of the existence of equilibrium other than DFE whenever $R_c < 1$. Furthermore, it can be shown that, the DFE P_1^0 of the model (2.8) is globally asymptotically stable (GAS) whenever $R_c < 1$.

From the above discussion we have concluded that

Theorem 3.3. *The model (2.8) has a unique endemic (positive) equilibrium, given by P^*, whenever $R_c > 1$ and has no endemic equilibrium for $R_c \leq 1$.*

Now we will prove the local stability of endemic equilibrium.

Theorem 3.4. *The endemic equilibrium P^* is locally asymptotically stable if $R_C > 1$.*

Proof. The Jacobian matrix of the system (2.8) $J_{P_1^0}$ at DFE is given by

$$J_{P_1^0} = \begin{bmatrix} -\mu & 0 & -r_Q\beta & -r_A\beta & -\beta & -r_J\beta & 0 \\ 0 & -(\gamma_1+k_1+\mu) & r_Q\beta & r_A\beta & \beta & r_J\beta & 0 \\ 0 & \gamma_1 & -(k_2+\sigma_1+\mu) & 0 & 0 & 0 & 0 \\ 0 & pk_1 & 0 & -(\sigma_2+\mu) & 0 & 0 & 0 \\ 0 & (1-p)k_1 & 0 & 0 & -(\gamma_2+\sigma_3+\mu) & 0 & 0 \\ 0 & 0 & k_2 & 0 & \gamma_2 & -(\delta+\sigma_4+\mu) & 0 \\ 0 & 0 & \sigma_1 & \sigma_2 & \sigma_3 & \sigma_4 & -\mu \end{bmatrix},$$

Here, we use the central manifold theory method to determine the local stability of the endemic equilibrium by taking β as bifurcation parameter [14]. Select β as the bifurcation parameter and gives critical value of β at $R_C = 1$ is given as

$$\beta^* = \frac{(\gamma_1+k_1+\mu)(k_2+\sigma_1+\mu)(\sigma_2+\mu)(\gamma_2+\sigma_3+\mu)(\delta+\sigma_4+\mu)}{[r_Q\gamma_1(\sigma_2+\mu)(\gamma_2+\sigma_3+\mu)(\delta+\sigma_4+\mu) + r_Apk_1(k_2+\sigma_1+\mu)(\gamma_2+\sigma_3+\mu)(\delta+\sigma_4+\mu) + Z]}$$

where, $Z = k_1(1-p)(k_2+\sigma_1+\mu)(\sigma_2+\mu)(\delta+\sigma_4+\mu) + r_J\gamma_1 k_2(\sigma_2+\mu)(\gamma_2+\sigma_3+\mu) + r_J(1-p)k_1\gamma_2(k_2+\sigma_1+\mu)(\sigma_2+\mu)$

The Jacobian of (2.8) at $\beta=\beta^*$, denoted by $J_{P_1^0}|_{\beta=\beta^*}$ has a right eigenvector (corresponding to the zero eigenvalue) given by $w=(w_1,w_2,w_3,w_4,w_5,w_6,w_7)^T$, where

$$w_1 = -\frac{\gamma_1+k_1+\mu}{\mu}w_2, w_2 = w_2 > 0, w_3 = \frac{\gamma_1}{k_2+\sigma_1+\mu}w_2, w_4 = \frac{pk_1}{\sigma_2+\mu}w_2,$$
$$w_5 = \frac{(1-p)k_1}{\gamma_2+\sigma_3+\mu}w_2, w_6 = \frac{k_2\gamma_1}{(\delta+\sigma_4+\mu)(k_2+\sigma_1+\mu)}w_2 + \frac{\gamma_2(1-p)k_1}{(\delta+\sigma_4+\mu)(\gamma_2+\sigma_3+\mu)}w_2$$
$$w_7 = \frac{1}{\mu}\Big[\frac{\sigma_1\gamma_1}{k_2+\sigma_1+\mu}w_2 + \frac{\sigma_2pk_1}{\sigma_2+\mu}w_2 + \frac{\sigma_3(1-p)k_1}{\gamma_2+\sigma_3+\mu]w_2} + \frac{\sigma_4k_2\gamma_1}{(\delta+\sigma+\mu)(k_2+\sigma_1+\mu)}w_2$$
$$+ \frac{\sigma_4\gamma_2(1-p)k_1}{(\delta+\sigma+\mu)(\gamma_2+\sigma_3+\mu)}w_2\Big].$$

Similarly, from $J_{P_1^0}|_{\beta=\beta^*}$, we obtain a left eigenvector $v=(v_1,v_2,v_3,v_4,v_5,v_6,v_7)^T$ (corresponding to the zero eigenvalue), where

$$v_1 = 0, v_2 = v_2 > 0, v_3 = \frac{r_Q\beta^*}{k_2+\sigma_1+\mu}v_2 + \frac{k_2r_J\beta^*}{(k_2+\sigma_1+\mu)(\delta+\sigma_4+\mu)}v_2, v_4 = \frac{r_A\beta^*}{\sigma_2+\mu}v_2,$$
$$v_5 = \frac{\beta^*}{\gamma_2+\sigma_3+\mu}v_2 + \frac{\gamma_2r_J\beta^*}{(\gamma_2+\sigma_3+\mu)(\delta+\sigma_4+\mu)}v_2, v_6 = \frac{r_J\beta^*}{\delta+\sigma_4+\mu}v_2, v_7 = 0.$$

Using the notations $S=x_1$, $E=x_2$, $Q=x_3$, $A=x_4$, $I=x_5$, $J=x_6$ and $R=x_7$. Hence, we have

$$a = \sum_{k,i,j=1}^{7} v_k w_i w_j \frac{\partial^2 f_k(0,0)}{\partial x_i \partial x_j}$$

and

$$b = \sum_{k,i=1}^{7} v_k w_i \frac{\partial^2 f_k(0,0)}{\partial x_i \partial \beta}$$

Replacing the values of all the second-order derivatives measured at DFE and $\beta=\beta^*$, we get

$$a = -\frac{2\beta^*\mu v_2}{\Pi}(r_Qw_3 + r_Aw_4 + w_5 + r_Jw_6)(w_2+w_4+w_5+w_7) < 0$$

and

$$b = v_2(r_Qw_3 + r_Aw_4 + w_5 + r_Jw_6) > 0$$

Since $a<0$ and $b>0$ at $\beta=\beta^*$, therefore using the Remark 1 of the Theorem 4.1 stated in [14], a transcritical bifurcation occurs at $R_C=1$ and the unique endemic equilibrium is locally asymptotically stable for $R_C>1$. □

3.5. ***Threshold analysis***

In this section the impact of quarantine and isolation is measured qualitatively on the disease transmission dynamics. A threshold study of the parameters correlated with the quarantine of exposed individuals $\gamma_1$and the isolation of the infected symptomatic individuals γ_2 is performed by measuring the partial derivatives of the control reproduction number R_c with respect to these parameters. We observe that

$$\frac{\partial R_c}{\partial \gamma_1} = \frac{r_Q\beta(k_1+\mu)}{(\gamma_1+k_1+\mu)^2(k_2+\sigma+\mu)} - \frac{r_A\beta p k_1}{(\gamma_1+k_1+\mu)^2(\sigma_2+\mu)} - \frac{\beta k_1(1-p)}{(\gamma_1+k_1+\mu)^2(\gamma_2+\sigma_3+\mu)} + \frac{r_J\beta}{(\gamma_1+k_1+\mu)^2(\gamma_2+\sigma_3+\mu)}\Big[\frac{k_2(k_1+\mu)}{k_2+\sigma_1+\mu} - \frac{(1-p)k_1\gamma_2}{\gamma_2+\sigma_3+\mu}\Big]$$

so that, $\frac{\partial R_c}{\partial \gamma_1} < 0\ (>0)$ iff $r_Q < r_{\gamma_1}\ (r_Q > r_{\gamma_1})$
where

$$0 < r_{\gamma_1} = \frac{k_2+\sigma_1+\mu}{k_1+\mu}\Big[\frac{r_A p k_1}{\sigma_2+\mu} + \frac{k_1(1-p)}{\gamma_2+\sigma_3+\mu}\Big] + \frac{r_J(k_2+\sigma_1+\mu)}{(k_1+\mu)(\delta+\sigma_4+\mu)}\Big[\frac{(1-p)k_1\gamma_2}{\gamma_2+\sigma_3+\mu} - \frac{k_2(k_1+\mu)}{k_2+\sigma_1+\mu}\Big]$$

From the previous analysis it is obvious that if the relative infectiousness of quarantine individuals r_Q will not cross the threshold value r_{γ_1}, then quarantining of exposed individuals results in reduction of the control reproduction number R_c and therefore reduction of the disease burden. On the other side, if $r_Q > r_{\gamma_1}$, then the control reproduction number R_c would rise due to the increase in the quarantine rate and thus the disease burden will also rise and therefore the use of quarantine in this scenario is harmful. The result is summarized in the following way:

Theorem 3.5. *For the model (2.8), the use of quarantine of the exposed individuals will have positive (negative) population-level impact if $r_Q < r_{\gamma_1}\ (r_Q > r_{\gamma_1})$.*

Similarly, measuring the partial derivatives of R_c with respect to the isolation parameter $\gamma_2$is used to determine the effect of isolation of infected symptomatic individuals. Thus, we obtain

$$\frac{\partial R_c}{\partial \gamma_2} = \frac{r_J\beta(1-p)k_1}{(\gamma_1+k_1+\mu)(\gamma_2+\sigma_3+\mu)(\delta+\sigma_4+\mu)} - \frac{r_J\beta(1-p)k_1\gamma_2}{(\gamma_1+k_1+\mu)(\gamma_2+\sigma_3+\mu)^2(\delta+\sigma_4+\mu)} - \frac{\beta k_1(1-p)}{(\gamma_1+k_1+\mu)(\gamma_2+\sigma_3+\mu)^2}$$

Thus, $\frac{\partial R_c}{\partial \gamma_2} < 0\ (>0)$ iff $r_J < r_{\gamma_2}\ (r_J > r_{\gamma_2})$
where

$$0 < r_{\gamma_2} = \frac{\delta+\sigma_4+\mu}{\sigma_3+\mu}$$

The use of isolation of infected symptomatic individuals will also be effective in controlling the disease in the population if the relative infectiousness of the isolated individuals r_J does not cross the threshold r_{γ_2}. The result is summarized below:

Theorem 3.6. *For the model (2.8), the use of isolation of infected symptomatic individuals will have positive (negative) population-level impact if* $r_J < r_{\gamma_2}$ $(r_J > r_{\gamma_2})$.

The control reproduction number R_c is a decreasing (non dcreasing) function of the quarantine and isolation parameters γ_1 and γ_2 if the conditions $r_Q < r_{\gamma_1}$ and $r_J < r_{\gamma_2}$ are respectively satisfied. See figure 8(a) and 8(b) obtained from model simulation in which the results correspond to the theoretical findings discussed.

3.6. ***Model without control and basic reproduction number***

We consider the system in this section when there is no control mechanism, that is, in the absence of quarantined and isolated classes. Setting $\gamma_1 = \gamma_2 = 0$ in the model (2.8) give the following reduce model

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \frac{S(\beta I + r_A \beta A)}{\hat{N}} - \mu S, \\
\frac{dE}{dt} &= \frac{S(\beta I + r_A \beta A)}{\hat{N}} - (k_1 + \mu)E, \\
\frac{dA}{dt} &= pk_1 E - (\sigma_2 + \mu)A, \\
\frac{dI}{dt} &= (1-p)k_1 E - (\sigma_3 + \mu)I, \\
\frac{dR}{dt} &= \sigma_2 A + \sigma_3 I - \mu R,
\end{aligned} \tag{3.6}$$

Where $\hat{N} = S + E + A + I + R$. The diseases-free equilibrium can be obtained for the system (3.6) by putting $E = 0, A = 0, I = 0$, which is denoted by $P_2^0 = (S^0, 0, 0, 0, R^0)$, where

$$S^0 = \frac{\Pi}{\mu}, R^0 = 0.$$

We will follow the convention that the basic reproduction number is defined in the absence of control measure, denoted by R_0 whereas we calculate the control reproduction number when the control measure are in the place. The basic reproduction number R_0 is defined as the expected number of secondary infections produced by a single infected individual in a fully susceptible population during his infectious period [11; 23; 29]. We calculate R_0 in the same way as we calculate R_c by using next generation operator method [48]. Now we calculate the jacobian of $\mathcal{F}$ and $\mathcal{V}$ at DFE P_2^0

$$F = \frac{\partial \mathcal{F}}{\partial X} = \begin{bmatrix} 0 & r_A\beta & \beta \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, V = \frac{\partial \mathcal{V}}{\partial X} = \begin{bmatrix} \gamma_1 + k_1 + \mu & 0 & 0 \\ -pk_1 & \sigma_2 + \mu & 0 \\ -(1-p)k_1 & 0 & \gamma_2 + \sigma_3 + \mu \end{bmatrix}.$$

Following [28], $R_0 = \rho(FV^{-1})$, where ρ is the spectral radius of the next-generation matrix (FV^{-1}). Thus, from the model (3.6), we have the following expression for R_0:

$$R_0 = \frac{r_A\beta p k_1}{(k_1+\mu)(\sigma_2+\mu)} + \frac{\beta k_1(1-p)}{(k_1+\mu)(\sigma_3+\mu)} \tag{3.7}$$

Thus, R_0 is R_c with $\gamma_1 = \gamma_2 = 0$.

3.6.1. ***Stability of DFE of the model 3.6***

Theorem 3.7. *The diseases free equilibrium (DFE) $P_2^0 = (S^0, 0, 0, 0, R^0)$ of the system (3.6) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. We calculate the Jacobian of the system (3.6) at DFE P_2^0, is given by

$$J_{P_2^0} = \begin{bmatrix} -\mu & 0 & -r_A\beta & -\beta & 0 \\ 0 & -(k_1+\mu) & r_A\beta & \beta & 0 \\ 0 & pk_1 & -(\sigma_2+\mu) & 0 & 0 \\ 0 & (1-p)k_1 & 0 & -(\sigma_3+\mu) & 0 \\ 0 & 0 & \sigma_2 & \sigma_3 & -\mu \end{bmatrix}$$

Let λ be the eigenvalue of the matrix $J_{P_2^0}$. Then the characteristic equation is given by $det(J_{P_2^0} - \lambda I) = 0$.

$$\Rightarrow r_A\beta p k_1(\lambda+\sigma_3+\mu)+\beta k_1[(1-p)(\lambda+\sigma_2+\mu)]-(\lambda+k_1+\mu)(\lambda+\sigma_2+\mu)(\lambda+\sigma_3+\mu) = 0.$$

which implies

$$\frac{r_A\beta p k_1}{(\lambda+k_1+\mu)(\lambda+\sigma_2+\mu)} + \frac{\beta k_1(1-p)}{(\lambda+k_1+\mu)(\lambda+\sigma_3+\mu)} = 1.$$

Denote

$$G_2(\lambda) = \frac{r_A\beta p k_1}{(\lambda+k_1+\mu)(\lambda+\sigma_2+\mu)} + \frac{\beta k_1(1-p)}{(\lambda+k_1+\mu)(\lambda+\sigma_3+\mu)}.$$

We rewrite $G_2(\lambda)$ as $G_2(\lambda) = G_{21}(\lambda) + G_{22}(\lambda)$
Now if $Re(\lambda) \geq 0$, $\lambda = x + iy$, then

$$|G_{21}(\lambda)| \leq \frac{r_A\beta p k_1}{|\lambda+k_1+\mu||\lambda+\sigma_2+\mu|} \leq G_{21}(x) \leq G_{21}(0)$$
$$|G_{22}(\lambda)| \leq \frac{\beta k_1(1-p)}{|\lambda+k_1+\mu||\lambda+\sigma_3+\mu|} \leq G_{22}(x) \leq G_{22}(0)$$

Then $G_{21}(0) + G_{22}(0) = G_2(0) = R_0 < 1$, which implies $|G_2(\lambda)| \leq 1$.
Thus for $R_0 < 1$, all the eigenvalues of the characteristics equation $G_2(\lambda) = 1$ has negative real parts.

Therefore if $R_0 < 1$, all eigenvalues are negative and hence DFE P_2^0 is locally asymptotically stable.

Now if we consider $R_0 > 1$ i.e $G_2(0) > 1$, then

$$\lim_{\lambda \to \infty} G_2(\lambda) = 0.$$

Then there exist $\lambda^* > 0$ such that $G_2(\lambda^*) = 1$.

That means there exist positive eigenvalue $\lambda^* > 0$ of the Jacobian matrix.

Hence DFE P_2^0 is unstable whenever $R_0 > 1$. □

Theorem 3.8. *The diseases free equilibrium (DFE) $P_2^0 = (S^0, 0, 0, 0, R^0)$ is globally asymptotically stable for the system (3.6) if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof. We rewrite the system (3.6)as

$$\frac{dX}{dt} = F_1(X, V)$$
$$\frac{dV}{dt} = G_1(X, V), G_1(X, 0) = 0$$

where $X = (S, R) \in R_2$ (the number of uninfected individuals compartments), $V = (E, A, I) \in R_3$ (the number of infected individuals compartments), and $P_2^0 = (\frac{\Pi}{\mu}, 0, 0, 0, 0)$ is the DFE of the system (3.6). The global stability of the DFE is guaranteed if the following two conditions are satisfied:

1. For $\frac{dX}{dt} = F_1(X, 0)$, X^* is globally asymptotically stable,
2. $G_1(X, V) = BV - \widehat{G}_1(X, V)$, $\widehat{G}_1(X, V) \geq 0$ for $(X, V) \in \hat{\Omega}$,

where $B = D_V G_1(X^*, 0)$ is a Metzler matrix and $\hat{\Omega}$ is the positively invariant set with respect to the model (3.6). Following Castillo-Chavez et al [13], we check for aforementioned conditions.
For system (3.6),

$$F_1(X, 0) = \begin{bmatrix} \Pi - \mu S \\ 0 \end{bmatrix},$$
$$B = \begin{bmatrix} -(k_1 + \mu) & r_A\beta & \beta \\ pk_1 & -(\sigma_2 + \mu) & 0 \\ (1-p)k_1 & 0 & -(\sigma_3 + \mu) \end{bmatrix}$$

and

$$\widehat{G}_1(X,V) = \begin{bmatrix} r_A\beta A(1-\frac{S}{N}) + \beta I(1-\frac{S}{N}) \\ 0 \\ 0 \end{bmatrix}.$$

Clearly, $\widehat{G}_1(X,V) \geq 0$ whenever the state variables are inside Ω. Also it is clear that $X^* = (\frac{\Pi}{d}, 0)$ is a globally asymptotically stable equilibrium of the system $\frac{dX}{dt} = F_1(X,0)$. Hence, the theorem follows. □

4. Model Calibration and epidemic potentials

We calibrated our 2019-nCoV model (2.8) to the daily new COVID cases for the five provinces of China namely Hubei, Guangdong, Henan, Zhejiang and Hunan. Daily COVID cases are collected for the period 22nd January, 2020- 21st February, 2020 from the official websites of the National Health Commission of China and Provincial Health Committees and World Health Organization [5; 1]. We fit the model (2.8) to daily new isolated cases of COVID in the five provinces. Due to the high transmissibility the notified cases are immediately isolated, and therefore it is convenient to fit the isolated cases to reported data. Also we fit the model (2.8) to cumulative isolated cases of COVID in those five provinces. We estimate the diseases transmission rates by humans, β , quarantine rate of exposed individuals, γ_1, isolation rate of infected individual, γ_2, rate at which quarantined individuals are isolated, k_2, recovery rate from quarantined individuals, σ_1, recovery rate from asymptomatic individuals, σ_2, recovery rate from isolated individuals, σ_4, and initial population sizes to match the COVID cases in five provinces of China. The COVID data are fitted using the Nonlinear Least Squares fitting routine lsqnonlin in the optimization tool box (MATLAB, R2017a). The estimated parameters are given in Table 3. We also estimate the initial conditions of the human population and the estimated values are given by Table 4. The fitting of the daily new isolated COVID cases in five provinces of China are displayed in Figure 2 and the fitting of the daily cumulative isolated cases are displayed in Figure 3.

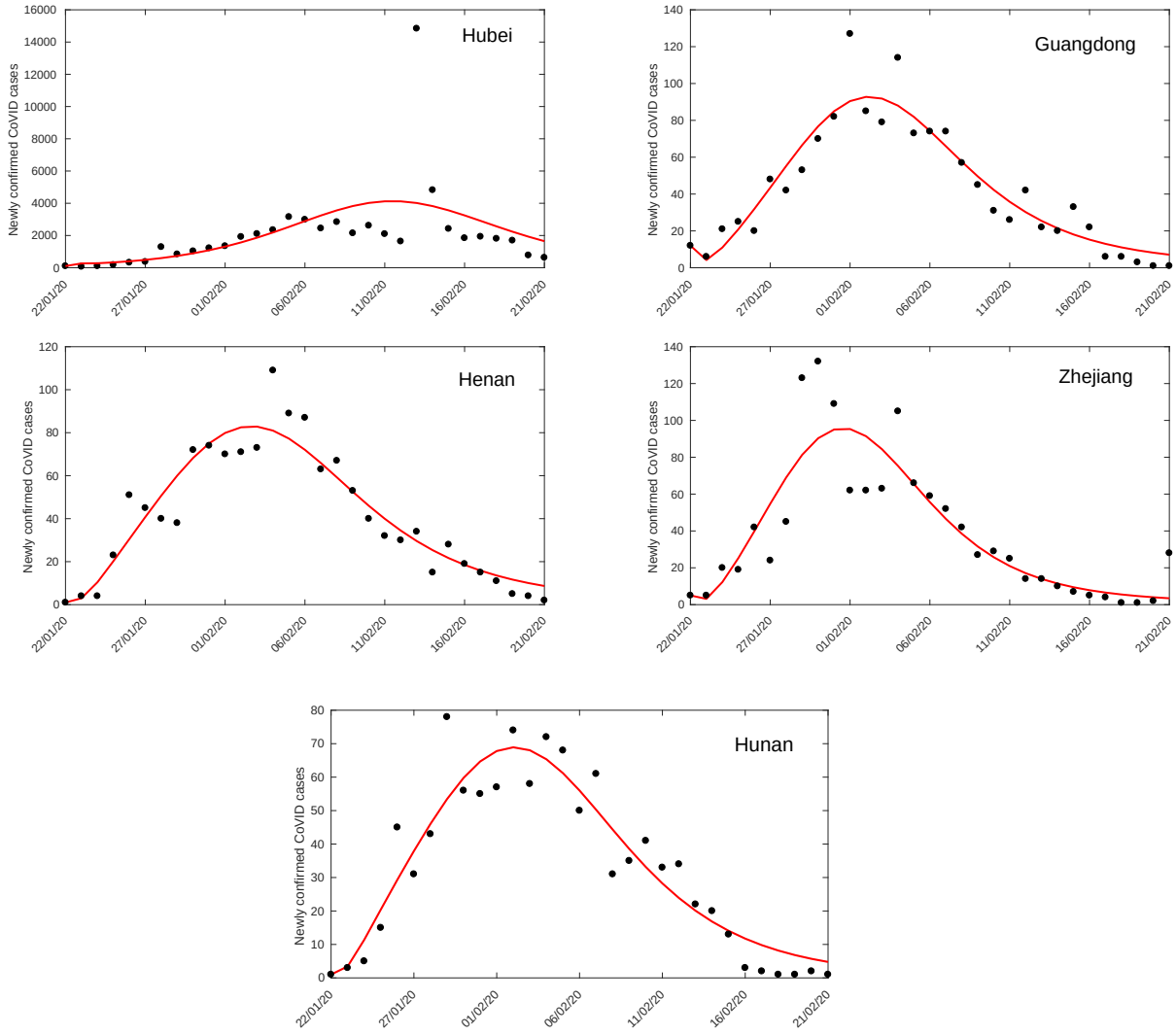

Figure 2: Model simulations fitted to daily new isolated COVID cases in (a) Hubei, (b) Guangdong, (c) Henan, (d) Zhejiang and (e) Hunan. Observed data points are shown in black circle and the solid red line depicts the model solutions.

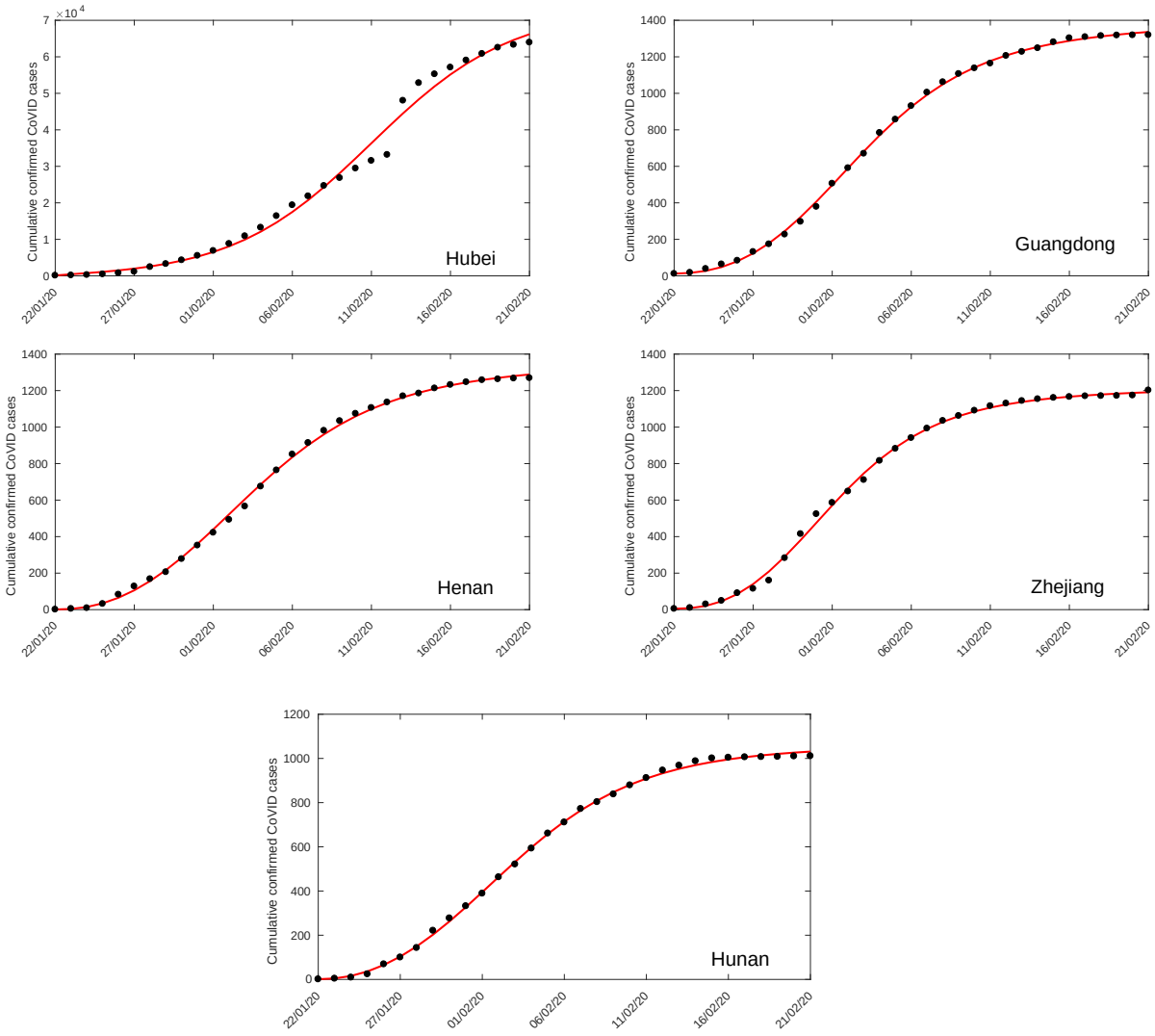

Figure 3: Model simulations fitted to daily cumulative isolated COVID cases in (a) Hubei, (b) Guangdong, (c) Henan, (d) Zhejiang and (e) Hunan. Observed data points are shown in black circle and the solid red line depicts the model solutions.

Table 2: Recruitment rates and disease induced mortality rates for the five provinces of China.

Parameters	Hubei	Guangdong	Henan	Zhejiang	Hunan
Π	2711	4072	3447	2059	2476
δ	0.034	0.00038	0.0157	0.00083	0.004

Table 3: Estimated parameters for the five provinces of China.

Parameters	Hubei	Guangdong	Henan	Zhejiang	Hunan
β	1.8457	1.6801	1.8344	1.6909	1.6646
γ_1	0.8570	0.8413	0.8478	0.9443	0.7097
γ_2	0.3249	0.0251	0.0177	0.0260	0.0196
k_2	0.0505	0.0000001	0.0000006	0.0000001	0.0000001
σ_1	0.3690	0.2633	0.2369	0.2222	0.3444
σ_2	0.2561	0.1741	0.4644	0.1503	0.1750
σ_4	0.2949	0.4755	0.4073	0.3558	0.6203

Table 4: Estimated initial population sizes for the five provinces of China.

Initial values	Hubei	Guangdong	Henan	Zhejiang	Hunan
$S(0)$	499980	160600	232730	172350	173950
$E(0)$	1147	17.89	905	110	31
$Q(0)$	1583	106	945	2001	37
$A(0)$	1.6	9704	9998	9798	9992
$I(0)$	914	77	386	1.4	14
$J(0)$	105	12	1	5	1
$R(0)$	280	85.7	0.5	23	175

Using these estimated parameters and the fixed parameters from Table 1, we calculate the basic reproduction numbers (R_0) and control reproduction numbers (R_c) for all of the five provinces. These estimates are given in Table 5

Table 5: Epidemic potentials of the five different provinces.

Reproduction number	Hubei	Guangdong	Henan	Zhejiang	Hunan
R_0	3.9098	3.7420	3.6956	3.8571	3.7045
R_c	2.0042	2.1695	2.5143	2.4845	1.8158

From Table 5, we observe that the estimated R_0 values matches with the previous estimates [52; 42; 7; 9; 51]. R_c values are all above unity, which indicates that these provinces should increase the control interventions to limit future COVID cases.

5. Short-term predictions

In this section, the short-term prediction capability of the model 2.8 is studied. Using estimated parameters form Tables 3 and 4, we simulate the newly isolated COVID cases

for the period 22nd February, 2020 - 12th March, 2020. All other fixed parameters are taken from Table 1 and 2. The short-term prediction for five provinces of China is depicted in Fig 4.

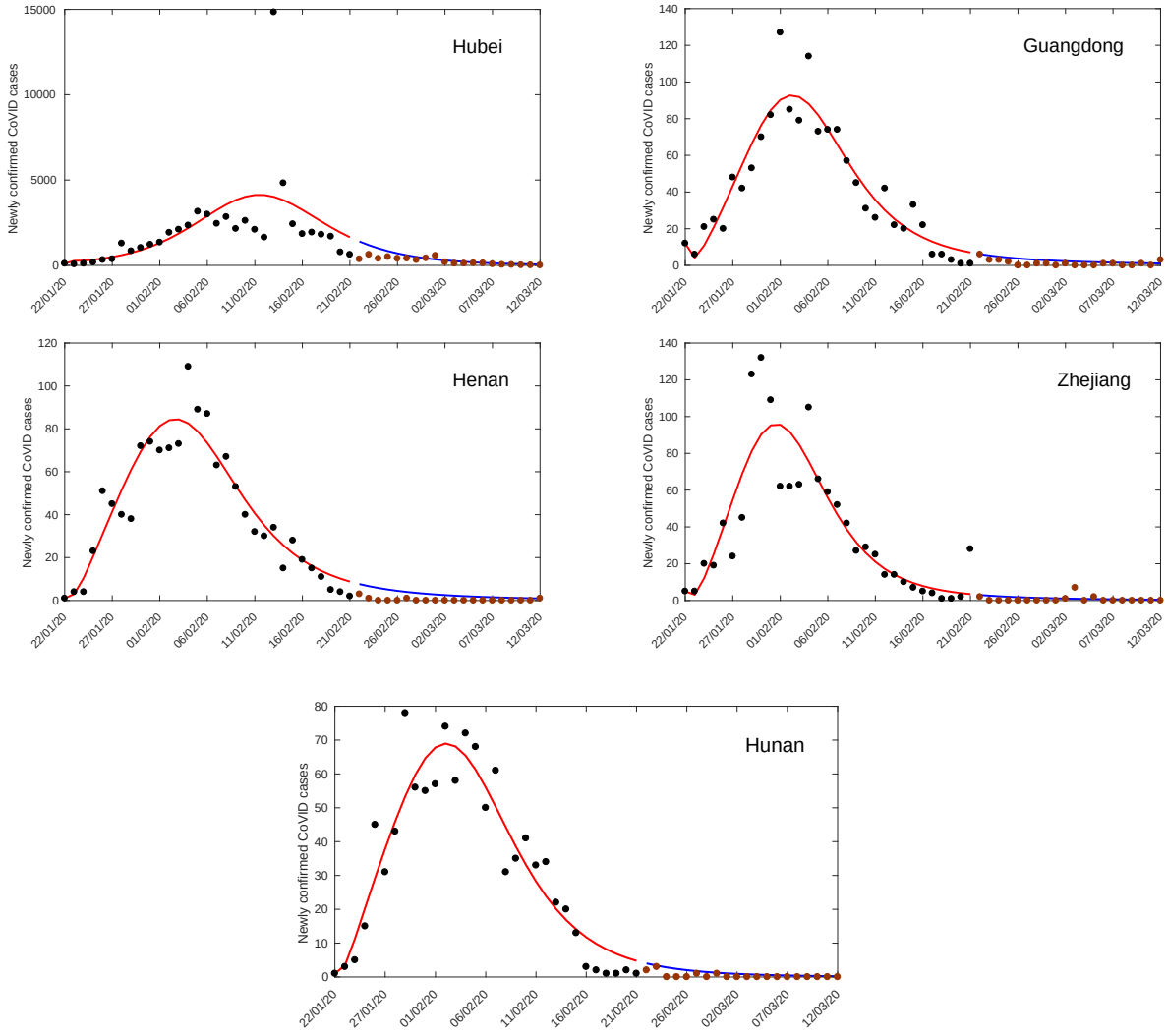

Figure 4: Short term predictions for the five provinces of China namely (a) Hubei, (b) Guangdong, (c) Henan, (d) Zhejiang and (e) Hunan. The blue line represent the predicted new isolated COVID cases while the solid dots are the actual cases. Here we have seen that the model performs excellently in case of five provinces namely Hubei, Guangdong, Henan, Zhejiang and Hunan and captured the decreasing trends of new COVID cases.

We calculate two performance metrics, namely Mean Absolute Error (MAE) and Root Mean Square Error (RMSE) to assess the accuracy of the predictions. This is defined using a set of performance metrics as follows:

Mean Absolute Error (MAE):

$$MAE = \frac{1}{N_p}\sum_{i=1}^{N_p}|Y(i) - \hat{Y}(i)|$$

Root Mean Square Error (RMSE):

$$RMSE = \sqrt{\frac{1}{N_p}\sum_{i=1}^{N_p}(Y(i) - \hat{Y}(i))^2}$$

where $Y(i)$ represent original cases, $\hat{Y(i)}$ are predicted values and N_p represents the sample size of the data. These performance metrics are reported in Table 6.

Table 6: Accuracy of the predictions in the five provinces.

Performance metrics	Hubei	Guangdong	Henan	Zhejiang	Hunan
MAE	220.7821	3.9570	2.9794	1.9114	1.9239
RMSE	332.5486	4.2188	3.2779	2.2472	2.1823

We found that the model performs excellently in case of four of the provinces namely Guangdong, Henan, Zhejiang and Hunan. On the other hand, the model performance is slightly worse for Hubei province compared to other provinces as the number of confirmed COVID cases are high. However, the decreasing trend of newly isolated COVID cases is well captured by the model for all the five provinces. Furthermore, to check the long term dynamics of the model we studied the time series. The short-term predictions displayed a decreasing trend but the values of R_c for each of the provinces were above unity. So, there may be a future outbreak in the long run. In Fig. 5, we plot the time series starting from 13 March, 2020 up-to 1000 days.

From Fig. 5, it can be observed that Hubei can experience future outbreaks if the control strategies are not implemented more efficiently. Sajadi et. al [44] assumed a seasonal pattern in the transmission dynamics of COVID and concluded that the COVID cases will amplify in the winter season. Our findings also indicate similar transmission patterns. The reason behind the endemicity of the disease is that $R_c > 1$, i.e., the DFE of the system is unstable. However, if the control measures are increased (or R_c is decreased below unity) and maintained efficiently, the subsequent outbreaks can be controlled.

6. Control strategies for Hubei province

In this section, we analyze sensitivity of model parameters with respect to the significant response variable, and analyze different control parameters to limit COVID cases

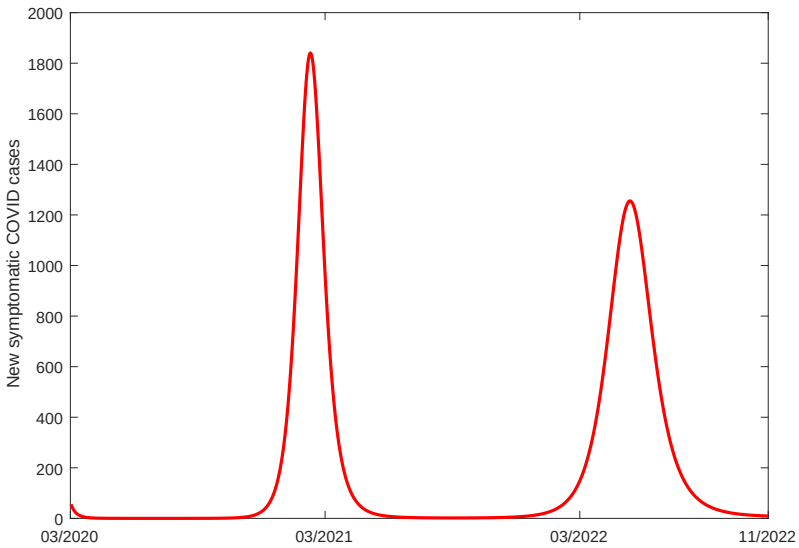

Figure 5: Long term prediction of new symptomatic infected cases in the Hubei province. Parameters and initial conditions are taken from Tables 1, 2 3 and 4

throughout Hubei province. In order to get an overview of most influential parameters, we compute the normalized sensitivity indices of the model parameters with respect to Rc. We have chosen parameters transmission rate between human population β, the control related parameters, γ_1, γ_2 and k_2, the recovery rates from quarantine individuals σ_1, asymptomatic individuals σ_2 and isolated individuals σ_4 and the effect of diseases induced mortality rate δ for sensitivity analysis. For the Hubei province, we compute normalized forward sensitivity indices of these parameters with respect to the control reproduction number R_c. We use the estimated parameters from Table 3 for the baseline values. The rest of the parameter values are the same as in Table 1 and Table 2. However, the mathematical definition of the normalized forward sensitivity index of a variable m with respect to a parameter τ (where m depends explicitly on the parameter τ) is given as:

$$X_m^\tau = \frac{\partial m}{\partial \tau} \times \frac{\tau}{m}.$$

The sensitivity indices of R_c with respect to the parameters β, γ_1, γ_2, k_2, σ_1, σ_2, σ_4 and δ are given by Table 7.

Table 7: Description of variables used in the model

$X_{R_c}^{\beta}$	$X_{R_c}^{\gamma_1}$	$X_{R_c}^{\gamma_2}$	$X_{R_c}^{k_2}$	$X_{R_c}^{\sigma_1}$	$X_{R_c}^{\sigma_2}$	$X_{R_c}^{\sigma_4}$	$X_{R_c}^{\delta}$
1.0000	-0.1194	-0.0097	0.0845	-0.6488	-0.0304	-0.2327	-0.0268

The fact that $X_{R_c}^{\beta} = 1$ means that if we increase 1% in β, keeping other parameters be fixed, will produce 1% increase in R_c. Similarly, $X_{R_c}^{\sigma_1} = -0.6488$ means increasing the parameter σ_1 by 1%, the value of R_c will be decrease by 0.6488% keeping the value of other parameters be fixed. Therefore, the transmission rate between susceptible humans and COVID infected humans is positively correlated and recovery rate from quarantined individuals is negatively correlated with respect to control reproduction number respectively.

In addition, we draw the contour plots of R_c with respect to the parameters γ_1 and γ_2 for the model (2.8) to investigate the effect of the control parameters on control reproduction number R_c, see Figure 6.

The contour plots of Figure 6 show the dependence of R_c on the quarantine rate γ_1 and the isolation rate γ_2 for the Hubei province. The axes of these plots are given as average days from exposed to quarantine $(1/\gamma_1)$ and average days from starting of symptoms to isolation $(1/\gamma_2)$. For both cases, the contours show that, increasing γ_1 and γ_2 reduces the amount of control reproduction number R_c and, therefore, COVID cases. For Hubei, using the parameters set from Table 1, 2, 3, 4 and $r_Q = 0.3$, we conclude that quarantine and isolation are not sufficient to control the outbreak (see Figure 6(a) and 6(c)). With these parameter values, as γ_1 increases, R_c decreases and similarly, when γ_2 increases, R_c decreases. But, in the both cases $R_c > 1$, and therefore the disease will persist in the population (i.e. the above control measures cannot lead to effective control of the epidemic). By contrast, our study shows that when the modification factor for quarantine become zero (so that $r_Q = 0$), the outbreak can be controlled (see Figure 6(b) and 6(d)). From the above finding it follows that neither the quarantine of exposed individuals nor the isolation of symptomatic individuals will prevent the disease with the high value of the modification factor for quarantine. This control can be obtained by a significant reduction in COVID transmission during quarantine (that is reducing rQ).

Furthermore, we study the effect of the parameters modification factor for quarantined individuals (r_Q), modification factor for isolated individuals (r_J) and transmission rate (β) on the newly infected symptomatic COVID cases (I_{cum}) in the Hubei province. The cumulative number of symptomatic cases has been computed at day 100 (chosen arbitrarily). The effect of controllable parameters on (I_{cum}) are shown in Fig. 7.

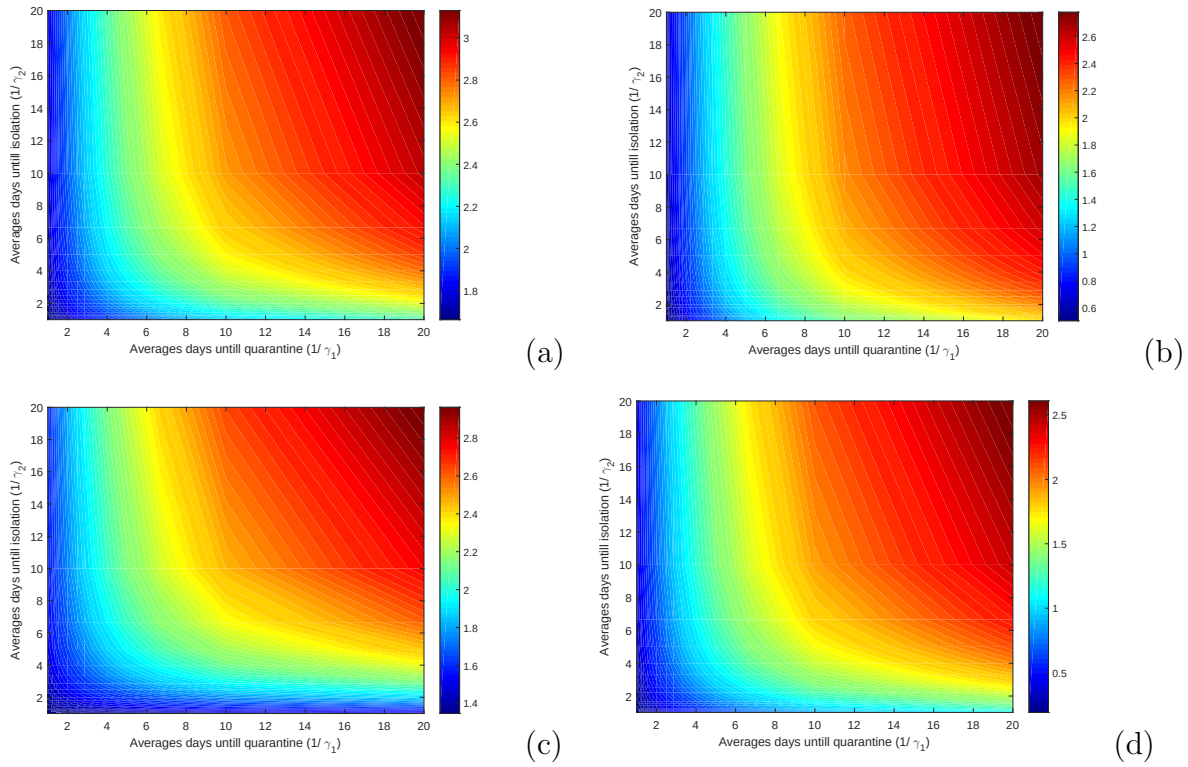

Figure 6: Contour plots of R_c versus average days to quarantine $(1/\gamma_1)$ and isolation $(1/\gamma_2)$ for the Hubei province, (a) in the presence of both modification factors for quarantined (r_Q) and isolation (r_J)(b) in the presence of modification factors for isolation (r_J) only (c) in the presence of modification factors for quarantined (r_Q) only and(d) in the absence of both modification factors for quarantined (r_Q) and isolation (r_J). All parameter values other than γ_1 and γ_2 are given in Table 3 for the Hubei province.

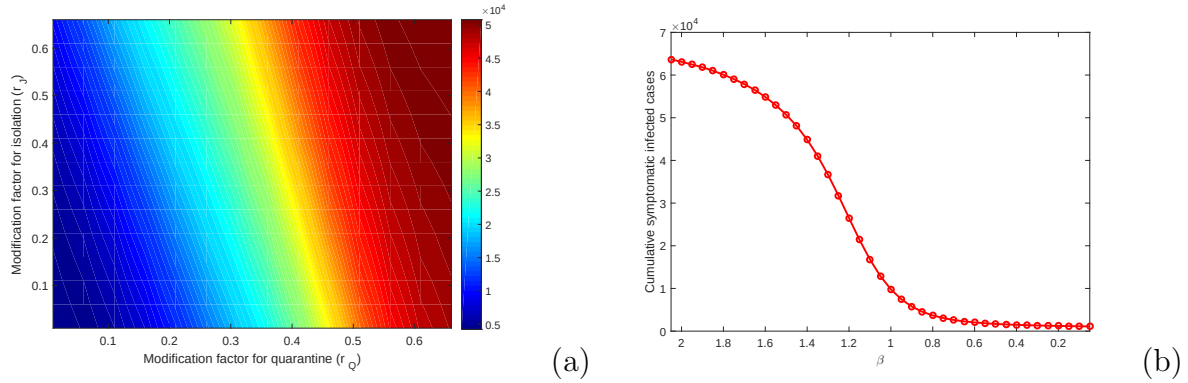

Figure 7: Effect of controllable parameters γ_1, γ_2 and β on the cumulative number of symptomatic infected COVID cases. The left panel shows the variability of the I_{cum} with respect to $\frac{1}{\gamma_1}$ and $\frac{1}{\gamma_2}$. The right panel shows I_{cum} with decreasing transmission rate β.

We observe that all the three parameters have significant effect on the cumulative

outcome of the epidemic. From Fig. 7(a) it is clear that decrease in the modification factor for quarantined and isolated individuals will significantly reduce the value of I_{cum}. On the other hand Fig. 7(b) indicates, reduction in transmission rate will also slow down the epidemic significantly. These results point out that all the three control measures are quite effective in reduction of the COVID cases in Hubei. Thus, quarantine and isolation efficacy should be increased by means of proper hygene and personal protection by health care stuffs. Additionally, the transmission coefficient can be reduced by avoiding contacts with suspected COVID infected cases.

Furthermore, We numerically calculated the thresholds r_{γ_1} and r_{γ_2} for Hubei province. The analytical expression of the thresholds are given in subsection (3.5). The effectiveness of quarantine and isolation depends on the values of the modification parameters r_Q and r_J for the reduction of infected individuals. The threshold value of r_Q corresponding to quarantine parameter γ_1 is $r_{\gamma_1} = 0.7439$ and the threshold value of r_J corresponding to isolation parameter γ_2 is $r_{\gamma_2} = 0.715$.

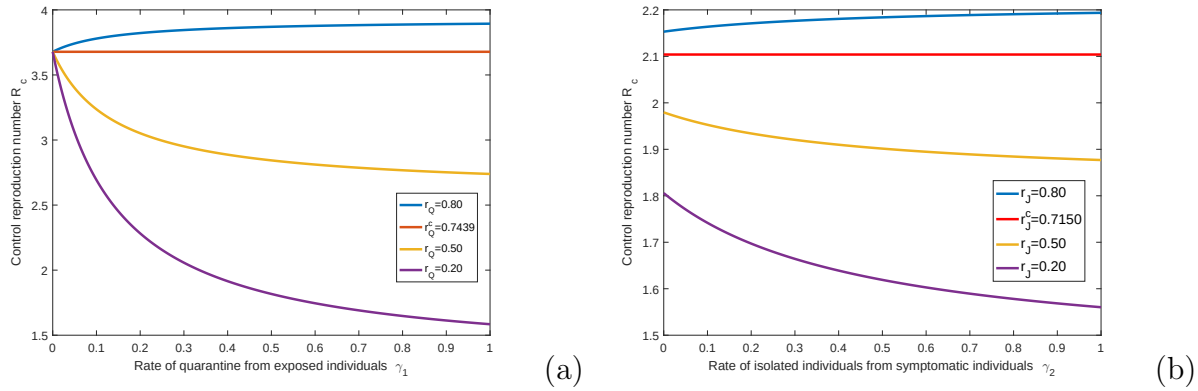

Figure 8: Effect of isolation parameters γ_1 and γ_2 on control reproduction number R_c.

From figure 8(a) it is clear that quarantine parameter γ_1 has positive population-level impact (R_c decreases with increase in γ_1) for $r_Q < 0.7439$ and have negative population level impact for $r_Q > 0.7439$. Similarly from the figure 8(b), it is clear that, isolation has positive level impact for $r_J < 0.715$, whereas isolation has negative impact if $r_J > 0.715$. This result indicate that isolation and quarantine programs should run effective so that the modification parameters remain below the above mentioned threshold.

7. Discussion

During the period of an epidemic when human-to-human transmission is established and reported cases of COVID are rising worldwide, forecasting is of utmost importance

for health care planning and control the virus with limited resource. In this study, we have formulated and analyzed a compartmental epidemic model of COVID to predict and control the outbreak. The basic reproduction number and control reproduction number are calculated for the proposed model. It is also shown that whenever $R_0 < 1$, the DFE of the model without control is globally asymptotically stable. The efficacy of quarantine of exposed individuals and isolation of infected symptomatic individuals depends on the size of the modification parameter to reduce the infectiousness of exposed (r_Q) and isolated (r_J) individuals. The usage of quarantine and isolation will have positive population-level impact if $r_Q < r_{\gamma_1}$ and $r_J < r_{\gamma_2}$ respectively. We calibrated the proposed model to fit daily data from five provinces of China namely, Hubei, Guangdong, Henan, Zhejiang and Hunan. Using the parameter estimates, we then found the basic and control reproducton numbers for these five provinces. Our findings suggest that independent self-sustaining human-to-human spread ($R_0 > 1$, $R_c > 1$) is already present in all the five provinces. The estimates of control reproduction number indicate that sustained control interventions are necessary to reduce the future COVID cases. The health care agencies should focus on successful implementation of control mechanisms to reduce the burden of the disease.

The calibrated model then checked for short-term predictability in the five provinces. It is seen that the model performs excellently in case of four of the provinces namely Guangdong, Henan, Zhejiang and Hunan while in case of Hubei, the model performance is slightly worse (Fig. 4). However, the decreasing trend of new COVID cases is well captured by the model for all the five provinces. The model predicted that all the five provinces will show decreasing trend of cases in the near future. But long term prediction show a oscillatory behaviour of disease incidence for Hubei province (Fig. 5). However, if the control measures are increased (or R_c is decreased below unity to ensure GAS of the DFE) and maintained efficiently, the subsequent outbreaks can be controlled.

Having an estimate of the parameters and prediction results, we concentrate on Hubei province for control intervention related numerical experiments. Sensitivity analysis reveal that the transmission rate is positively correlated and quarantine and isolation rates negatively correlated with respect to control reproduction number. This indicate that increasing quarantine and isolation rates and decreasing transmission rate will decrease the control reproduction number and consequently will reduce the disease burden.

While investigating the contour plots 6, we found that effective management of quarantined individuals is more effective that management of isolated individuals to reduce the control reproduction number below unity. Thus if limited resources are available, then investing on the quarantined individuals will be more fruitful in terms of reduction of cases.

Finally, we studied the effect of modification factor for quarantined population, modification factor for isolated population and transmission rate on the newly infected symp-

tomatic COVID cases in the Hubei province. Numerical results show that all the three control measures are quite effective in reduction of the COVID cases in Hubei (Fig. 7). The threshold analysis reinforce that the quarantine and isolation efficacy should be increased to reduce the epidemic in Hubei (Fig. 8). Thus, quarantine and isolation efficacy should be increased by means of proper hygene and personal protection by health care stuffs. Additionally, the transmission coefficient can be reduced by avoiding contacts with suspected COVID infected cases.

In summary, our study suggests that COVID has a potential to show oscillatory behaviour in the future but it is controllable by social distancing measures and efficiency in quarantine and isolation. The ongoing control interventions should be adequately funded and monitored. Health care officials should supply medications, protective masks and necessary human resources in the affected areas.

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