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OPTIMAL CONTROL ANALYSIS FOR THE MERS-COV OUTBREAK: SOUTH KOREA PERSPECTIVES

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ABSTRACT. This paper presents the mathematical model for the MERS-CoV outbreak in South Korea, and the optimal control for two intervention strategies (contact, hospitalization) is implemented. After the MERS-CoV outbreak, hospitalizing infected individuals did not help to prevent the spread of infection. However, the intervention to control contact was effective. It was effective the intervention to controlling both of contact and hospitalization of infection population.

1. INTRODUCTION

Middle East respiratory syndrome(MERS) is a viral respiratory disease caused by a novel coronavirus (Middle East respiratory syndrome coronavirus, or MERS-CoV) that was first identified in Saudi Arabia in 2012. MERS-CoV is a zoonotic virus; that is, it is transmitted between animals and people. Studies have shown that humans are infected by direct or indirect contact with infected dromedary camels [17]. Close contact between a person and an infected camel appears to be necessary for the transmission of MERS-CoV. It has been suggested that the virus could infect humans through the air [16]. Mathematical modeling for disease transmission has been done by many different authors to understand the dynamic spread of disease in humans. The case of the MERS-CoV Drosten et al [7] provide a description of a fatal case of MERS-CoV infection and associated phylogenetic analyses. Guery et al [9] analyzed the clinical features of infected cases, and Memish et al [12] and Al-Tawfiq et al [1] described the epidemiological data in terms of family clusters and hospitalized patient, respectively.

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After MERS was first reported in Saudi Arabia in 2012, an outbreak of Middle East respiratory syndrome coronavirus occurred in South Korea from May to July 2015. The number of patients with MERS-CoV increased explosively in several hospitals in South Korea that were not familiar with the symptoms of MERS. For Koreans, the prevalence of the infection was shocking, because South Korea has advanced medical and public health systems. However, some of hospitals became part of the route of the infection, even though the hospitals were advanced medical centers. The best description of MERS-CoV in South Korea is presented by Korea Centers for Disease Control and Prevention [11], although it was briefly mentioned by Chowell et al [4] and Cho and Chu [2]. [15] formulated a mathematical model for MERS transmission dynamics and estimating transmission rates. They estimated the basic reproduction number using the estimates of the transmission rates, in the first two periods.

Our aim is to minimize the MERS-CoV transmission. We present a mathematical model for the dynamics of MERS-CoV transmission, including an asymptomatic class, as well as strategies to reduce infections by means of two mechanisms: reducing the close contact rate and increasing the hospitalized cases.

Numerical simulations show control strategies for MERS-CoV transmission in South Korea. In Section 2, we formulate a mathematical model, and Section 4 presents numerical results based on optimal control of the spread in Section 3. Conclusions are presented in the final section.

2. Mathematical Modeling

Our model of MERS-CoV transmission is based on the model in Yunhwan et al [15] and Chowell et al [3], and deals with the outbreak in South Korea.

The model uses six epidemiological classes. Each individual is in one of the six classes. The classes are: susceptible S, exposed (or high-risk latent) E, symptomatic and infectious I, infected but asymptotic A, hospitalized H, and recovered R. It is assumed that only infectious and hospitalized individuals can infect others and asymptomatic individuals also can.

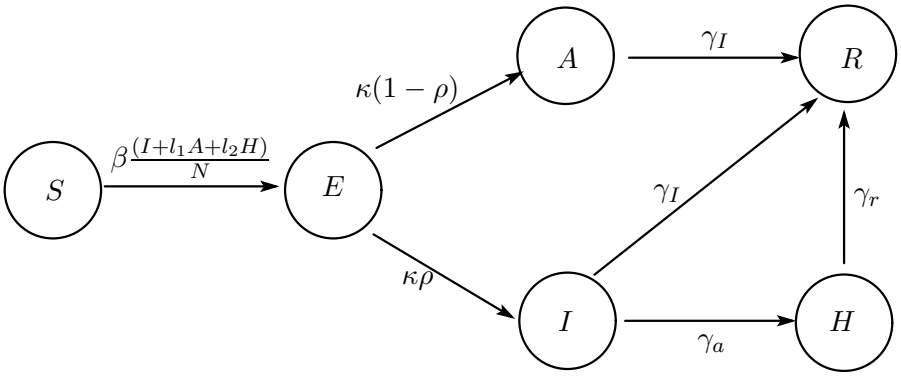

FIGURE 1. A transmission diagram of individuals in the different epidemiological classes in our model.

In Chowell et al [3], the actual data of the zoonotic cases were gathered so they were able to take secondary cases as well as index cases into account. The model of [15] considered a MERS-CoV model without the zoonotic case. Meanwhile, we added the susceptible class and infection but asymptotic class A to the model [15] because asymptomatic individuals can infect susceptible people. With the given assumptions and the illustration in Fig. 1, we obtain the following six-dimensional system of nonlinear differential equations;

$$\begin{aligned}
\frac{dS}{dt} &= -\beta\frac{(I + l_1A + l_2H)}{N}S,\\
\frac{dE}{dt} &= \beta\frac{(I + l_1A + l_2H)}{N}S - \kappa E,\\
\frac{dI}{dt} &= \kappa\rho E - (\gamma_a + \gamma_I)I,\\
\frac{dA}{dt} &= \kappa(1-\rho)E - \gamma_I A,\\
\frac{dH}{dt} &= \gamma_a I - \gamma_r H,\\
\frac{dR}{dt} &= \gamma_I I + \gamma_r H + \gamma_I A.
\end{aligned} \tag{2.1}$$

Where $N = S + E + I + A + H + R$.

Here β is the human-to-human transmission rate per unit of time, l_1 and l_2 quantify the relative transmissibility of infection by the asymptomatic class and hospitalized patients, respectively; κ is the rate at which an individual leaves the exposed class by becoming infectious (symptomatic or asymptomatic); ρ is the proportion of progression from exposed class E to symptomatic infectious class I, and $(1-\rho)$ is that of progression to asymptomatic class A; γ_a is the average rate at which symptomatic individuals are hospitalized and γ_I is the recovery rate without being hospitalized; γ_r is the recovery rate of hospitalized patients.

The variable domain of the model is

$$\Omega = \{(S, E, I, A, H, R) \in \mathbb{R}^6 | S, E, I, A, H, R \geq 0\}.$$

All parameters used in the model; $\beta, l_1, l_2, \kappa, \rho, 1-\rho, \gamma_a, \gamma_r$ and γ_I are positive. It can be verified that Ω is a positively invariant set with respect to the model. The model (2.1) has two equilibrium points which are given by $(S, E, I, A, H, R) = (0, 0, 0, 0, 0, 0)$ and $(S, E, I, A, H, R) = (S, 0, 0, 0, 0, R)$.

For the prevalence of the disease, the basic reproductive number tells us whether the disease will persist or disappear, so we consider the basic reproductive number.

2.1. **Basic Reproductive Number.** The dynamic behavior of the model can be classified by the basic reproductive number. This threshold condition determines whether an infectious disease will spread in a susceptible population when the disease is introduced into the population [10]. The threshold is calculated by using the spectral radius of a next-generation (infection)

matrix of a model [6]. It is given mathematically as

$$\mathcal{R}_0 = \rho(FV^{-1}),$$

where ρ is defined as the spectral radius of the next- generation matrix FV^{-1}. $\mathcal{F}$ is the rate of appearance of new infections in class i, and $\mathcal{V}$ is the transfer of individuals out of class i by all other means. Then, we find the Jacobian matrix of $\mathcal{F}(x)$ and $\mathcal{V}(x)$, and denote $F = [\partial\mathcal{F}_i/\partial x_j]$ and $V = [\partial\mathcal{V}_i/\partial x_j]$ evaluated at the disease free equilibrium point E_0, which consists of $S = N$. From the spectral radius, we get $\mathcal{R}_0$ as following;

$$\mathcal{R}_0 = \beta\left(\frac{\rho}{\gamma_a+\gamma_I} + \frac{\rho\gamma_a l_2}{\gamma_r(\gamma_a+\gamma_I)} + \frac{(1-\rho)l_1}{\gamma_I}\right) \tag{2.2}$$

As shown in (2.2), the basic reproductive number of system (2.1) depends on parameters $\beta, l_1, l_2, \gamma_r, \rho, \gamma_I$, and γ_a. The disease-free equilibrium point will be locally asymptomatically stable iff $\mathcal{R}_0 < 1$. The basic reproductive number $\mathcal{R}_0$ measures how quickly a disease spreads in its initial phase as well as predicts whether a disease will become endemic or whether it will die out.

Sensitivity indices allow us to measure the relative change in a variable when a parameter changes. By the use $\mathcal{R}_0$, the sensitivities are parameters; β, γ_a, i.e,

$$S_\beta = \frac{\partial\mathcal{R}_0}{\partial\beta}\frac{\beta}{\mathcal{R}_0} = 1,$$

$$S_{\gamma_a} = \frac{\partial\mathcal{R}_0}{\partial\gamma_a}\frac{\gamma_a}{\mathcal{R}_0} = \frac{\gamma_a\rho(\gamma_I l2 - \frac{1}{(\gamma_a+\gamma_I)^2})}{\frac{\rho}{(\gamma_a+\gamma_I)} - \frac{l2(\rho-1)}{\gamma_I} + \frac{(\gamma_a l2\rho)}{\gamma_r(\gamma_a+\gamma_I)}}.$$

The value of $\mathcal{R}_0$ could be reduced by reducing β and increasing γ_a.

The application of control measures changes of some parameter values in the model; moreover we would need to know the effects that the changes produce on $\mathcal{R}_0$ for control. The control variables $0 \le u_1(t) \le 1$ and $0 \le u_2(t) \le 1$ represent the amount of intervention at time t to reduce the contact rate β and to increase hospitalization γ_a.

Since the infection shapes a large cluster in a hospital, we consider the parameters related to hospital and contact with asymptomatic classes.

3. MERS-CoV Optimal Control Analysis

For the outbreak of MERS-CoV in South Korea, the infection shapes a large cluster in a hospital. Tracing the movements of patients at a South Korean hospital has helped identify how the Middle East Respiratory Syndrome (MERS) virus was transmitted from a patient to individuals(including patients, visitors and health-care workers) in an overcrowded emergency room. In this section, we carry out optimal control analysis which focuses on the two intervention strategies(contact, hospitalization) considered in the model (3.1). The idea of adding control terms was inspired by the model of Y. Kim et al [15].

Now we formulate an optimal control problem for the transmission dynamics of MERS-CoV in South Korea. We add control terms to the our model (2.1). The model (2.1) is re-formulated

as an optimal control problem as follows;

$$\begin{aligned}
\frac{dS}{dt} &= -\beta(1-u_1(t))\frac{(I+l_1A+l_2H)}{N}S,\\
\frac{dE}{dt} &= \beta(1-u_1(t))\frac{(I+l_1A+l_2H)}{N}S-\kappa E,\\
\frac{dI}{dt} &= \kappa\rho E-\gamma_I I-\gamma_a(1+\omega u_2(t))I,\\
\frac{dA}{dt} &= \kappa(1-\rho)E-\gamma_I A,\\
\frac{dH}{dt} &= \gamma_a(1+\omega u_2(t))I-\gamma_r H,\\
\frac{dR}{dt} &= \gamma_I I+\gamma_r H+\gamma_I A.
\end{aligned} \tag{3.1}$$

The control variable $u_1(t)$ represents the number of interventions needed to reduce the contact rate at time t. After control, the contact rate is $(1-u_1(t))$ where $u_1(t)$ measures the level of successful prevention efforts. The control variable $u_2(t)$ represents efforts to increase the hospitalization rate. It is assumed that the hospitalization rate increases at a rate proportional to $u_2(t)$ and where ω is a rate constant.

We show that it is possible to implement time dependent control $u_1(t)$ and $u_2(t)$ while minimizing the cost of implementation of such control measures.

We define the set of admissible controls as follows;

$$\mathcal{U} = \{(u_1(t), u_2(t)) | u_1(t), u_2(t) \text{ are Lebesgue measurable on } [0,T], 0 \le u_1(t), u_2(t) \le 1\}$$

where T is the final time.

Focusing the optimal control problem on minimizing the number of contacts and hospitalized individuals the problem reduces to minimizing the cost functional. To specify the cost, we define the cost functional as

$$J(u_1,u_2) = \int_0^T \left\{ A_1 I(t) + A_2 A(t) + A_3 H(t) + \frac{B_1}{2}u_1^2(t) + \frac{B_2}{2}u_2^2(t) \right\} dt \tag{3.2}$$

subject to the differential equations (3.1).

In the objective functional the quantities A_1, A_2, and A_2 represent the weight constants of the symptomatic infectious class, asymptomatic class, and hospitalized individuals, respectively. In the objective functional, the weight coefficients B_1 and B_2 are constants that represent cost. The terms $\frac{1}{2}B_1u_1^2$ and $\frac{1}{2}B_2u_2^2$ describe the costs associated with the transmission by contact rate with the susceptible individuals and hospitalization for minimizing the symptomatic infectious individuals, respectively.

3.1. **Existence of an Optimal Control.** The necessary condition, to be satisfied by the control and the corresponding states, is derived using Pontryagin's Maximum Principle [13]. Using the

differential equation of the state variable of the model (3.1), the Hamiltonian is given by:

$$\begin{aligned}
&\mathcal{H}(\mathbf{X}(t),\mathcal{U}(t),\mathbf{\Lambda}(t))\\
=&A_1I(t)+A_2A(t)+A_3H(t)+\frac{B_1}{2}u_1^2(t)+\frac{B_2}{2}u_2^2(t)+\mathbf{\Lambda}(t)\left(\frac{d\mathbf{X}(t)}{dt}\right)^T\\
=&A_1I(t)+A_2A(t)+A_3H(t)+\frac{B_1}{2}u_1^2(t)+\frac{B_2}{2}u_2^2(t)\\
&+\lambda_1\left\{-\beta(1-u_1(t))\frac{(I+l_1A+l_2H)}{N}S\right\}\\
&+\lambda_2\left\{\beta(1-u_1(t))\frac{(I+l_1A+l_2H)}{N}S-\kappa E\right\}\\
&+\lambda_3\left\{\kappa\rho E-\gamma_II-\gamma_a(1+\omega u_2)I\right\}\\
&+\lambda_4\left\{\kappa(1-\rho)E-\gamma_IA\right\}\\
&+\lambda_5\left\{\gamma_a(1+\omega u_2(t))I-\gamma_rH\right\}\\
&+\lambda_6\left\{\gamma_II+\gamma_rH+\gamma_IA\right\},
\end{aligned}\tag{3.3}$$

where $\lambda_j(j=1,2,...,6)$ are the adjoint variables and the state variables for the population dynamics are denoted by $\mathbf{X}(t)=(S(t),I(t),E(t),A(t),H(t),R(t))$, the existence of which is guaranteed by the Pontryagin's Maximum Principle [14].

Our goal is to find optimal controls $u_1^*(t)$ and $u_2^*(t)$ such that

$$J(u_1^*,u_2^*)=\min\{J(u_1,u_2)|(u_1,u_2)\in\mathcal{U}\}.\tag{3.4}$$

Such optimal control functions u_1^* and u_2^* exist and the optimality system can be derived, and which satisfy conditions summarized in the following theorem:

Theorem 3.1. *Let $S^*(t),E^*(t),I^*(t),A^*(t),H^*(t)$ and $R^*(t)$ be optimal state solutions with associated optimal control variables u_1^* and u_2^* for the optimal control problem (3.1) and (3.2), then there exists an adjoint variable $\mathbf{\Lambda}(t)=(\lambda_1(t),\lambda_2(t),\lambda_3(t),\lambda_4(t),\lambda_5(t),\lambda_6(t))$ that satisfies*

$$\begin{aligned}
\lambda_1'&=\frac{\beta(1-u_1(t))(I+l_1A+l_2H)}{N}(\lambda_1-\lambda_2)\\
\lambda_2'&=\lambda_2\kappa-\lambda_3\kappa\rho-\lambda_4\kappa(1-\rho)\\
\lambda_3'&=-A_1+\frac{\beta(1-u_1(t))S}{N}(\lambda_1-\lambda_2)+\gamma_a(1+\omega u_2)(\lambda_3-\lambda_5)+\\
&\quad\gamma_I(\lambda_3-\lambda_6)\\
\lambda_4'&=-A_2+\frac{\beta(1-u_1(t))l_1S}{N}(\lambda_1-\lambda_2)+\gamma_I(\lambda_4-\lambda_6)\\
\lambda_5'&=-A_3+\frac{\beta(1-u_1(t))l_2S}{N}(\lambda_1-\lambda_2)+\gamma_r(\lambda_5-\lambda_6)\\
\lambda_6'&=0
\end{aligned}\tag{3.5}$$

with transversality conditions (or boundary conditions)

$$\lambda_j(T) = 0, j = 1, 2, ..., 6.$$

Furthermore, the optimal controls u_1^* and u_2^* are given by

$$\begin{aligned} u_1^*(t) &= \min\left\{1, \max\left\{0, \frac{\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1)}{N B_1}\right\}\right\}, \\ u_2^*(t) &= \min\left\{1, \max\left\{0, \frac{\gamma_a \omega I^*(\lambda_3 - \lambda_5)}{B_2}\right\}\right\}. \end{aligned} \tag{3.6}$$

Proof. To determine the adjoint equations and the transversality conditions, we use the Hamiltonian (3.3). By Pontryagin's Maximum Principle, $S(t) = S^*(t), E(t) = E^*(t), I(t) = I^*(t)$, $A(t) = A^*(t), H(t) = H^*(t)$ and $R(t) = R^*(t)$, and also differentiating the Hamiltonian (3.3) with respect to $S(t), E(t), I(t), A(t), H(t)$ and $R(t)$, we obtain

$$\begin{aligned} \lambda_1' &= -\frac{\partial \mathcal{H}}{\partial S} = \frac{\beta(1 - u_1^*(t)(I^* + l_1 A^* + l_2 H^*)}{N}(\lambda_1 - \lambda_2) \\ \lambda_2' &= -\frac{\partial \mathcal{H}}{\partial E} = \lambda_2 \kappa - \lambda_3 \kappa \rho - \lambda_4 \kappa(1 - \rho) \\ \lambda_3' &= -\frac{\partial \mathcal{H}}{\partial I} = -A_1 + \frac{\beta(1 - u_1^*(t))S^*}{N}(\lambda_1 - \lambda_2) + \gamma_a(1 + \omega u_2)(\lambda_3 - \lambda_5) + \\ &\qquad \gamma_I(\lambda_3 - \lambda_6) \\ \lambda_4' &= -\frac{\partial \mathcal{H}}{\partial A} = -A_2 + \frac{\beta(1 - u_1^*(t))l_1 S^*}{N}(\lambda_1 - \lambda_2) + \gamma_I(\lambda_4 - \lambda_6) \\ \lambda_5' &= -\frac{\partial \mathcal{H}}{\partial H} = -A_3 + \frac{\beta(1 - u_1^*(t))l_2 S^*}{N}(\lambda_1 - \lambda_2) + \gamma_r(\lambda_5 - \lambda_6) \\ \lambda_6' &= -\frac{\partial \mathcal{H}}{\partial R} = 0. \end{aligned} \tag{3.7}$$

To obtain the optimality condition (3.6), we also differentiate the Hamiltonian $\mathcal{H}$ with respect to u_1 and u_2 and set each of them equal to zero.

$$\begin{aligned} 0 &= \frac{\partial \mathcal{H}}{\partial u_1} = B_1 u_1^* + \frac{S^* \beta(I^* + l_1 A^* + l_2 H^*)}{N}(\lambda_1 - \lambda_2), \\ 0 &= \frac{\partial \mathcal{H}}{\partial u_2} = B_2 u_2^* + \gamma_a \omega I^*(\lambda_5 - \lambda_3). \end{aligned}$$

Solving for the optimal controls, we obtain

$$\begin{aligned} u_1^* &= \frac{\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1)}{N B_1}, \\ u_2^* &= \frac{\gamma_a \omega I^*(\lambda_3 - \lambda_5)}{B_2}. \end{aligned}$$

To determine an explicit expression for the optimal controls for $0 \leq u_1^* \leq 1$ and $0 \leq u_2^* \leq 1$, we utilized a standard optimality technique. We consider the following three cases.

Case 1. On the set $\{t \mid 0 < u_1^* < 1\}$, we have $\dfrac{\partial \mathcal{H}}{\partial u_1} = 0$.

Hence the optimal control is

$$u_1^* = \frac{\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1)}{NB_1}.$$

Case 2. On the set $\{t \mid u_1^*(t) = 0\}$, we have $\dfrac{\partial \mathcal{H}}{\partial u_1} \geq 0$.

This implies that

$$\begin{aligned} &-\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1) \geq 0 \\ \Rightarrow\ &\frac{\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1)}{NB_1} \leq 0 = u_1^*(t). \end{aligned}$$

Case 3. On the set $\{t \mid u_1^*(t) = 1\}$. we have $\dfrac{\partial \mathcal{H}}{\partial u_1} \leq 0$.

This implies that

$$\begin{aligned} &-\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1) \leq -B_1 \\ \Rightarrow\ &\frac{\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1)}{NB_1} \geq 1 = u_1^*(t). \end{aligned}$$

Combining these three cases above, we find a characterization of u_1^*:

$$u_1^* = \min\left\{1, \max\left\{0, \frac{\beta S^*(I^* + l_1 A^* + l_2 H^*)(\lambda_2 - \lambda_1)}{NB_1}\right\}\right\}.$$

Using the same arguments, we also obtain the second optimal control function

$$u_2^*(t) = \min\left\{1, \max\left\{0, \frac{\gamma_a \omega I^*(\lambda_3 - \lambda_5)}{B_2}\right\}\right\}.$$

□

4. Numerical Simulations

The system (3.1) is solved numerically using Forward-Backward Sweep Method [14] to deduce optimal controls u_1^* and u_2^* that minimize the cost functional (3.2). Here, we use numerical simulations to illustrate the effectiveness of optimal controls using the parameters values mentioned in Table 1.

The effectiveness of the control measures are not always the same. Further, the controls could not be 100% effective. So, the upper bounds of u_1^* and u_2^* were chosen to be 0.6.

To imitate the onset of the disease outbreak, we first consider a collection of $10,000$ individuals including two infected individuals. The control scenario along with the optimal solutions is presented in Figs. 2, 3, and 4. The horizontal axis is the time measured in days and shows the start of the 2015 MERS-CoV outbreak in South Korea. The graph on the left of each figure shows the control scenario. Here, the dotted line is the control u_2^* and the solid line is the

TABLE 1. The description and values of parameters for the model

Parameter	Description	Value	Refs
β	Human-to-human transmission rate	0.0835	[15]
l_1	Quantifies the relative transmissibility of asymptomatic class	0.2	[15]
l_2	Quantifies the relative transmissibility of patients	22	[15]
κ	Rate at which an individual leaves E class by becoming infectious	1/(6.6)	[8]
ρ	The proportion of progression from class E to I class	0.585	[5]
γ_a	Average rate at which symptomatic individuals hospitalize	0.6403	[5]
γ_I	Average recovery rate without being hospitalized in I class	1/5	[5]
γ_r	The recovery rate of hospitalized patients	1/7	[5]

control u_1^*. The state variables are presented in the graph on the right. Here, the dotted line represents the state variables with control and the solid line represents the state variables without control. The outbreak of MERS-CoV occurred in South Korea from May to July 2015, and was completely finished by November 2015. The duration of the epidemic was about 180 days and about $12,208$ individuals were quarantined.

In Fig. 2, we considered no intervention ($u_1^* = 0$) only hospitalization ($0 \leq u_2^* \leq 0.6$). The optimal control scenario and the corresponding solution of the state variables S, E, I, A, H, R are shown on the graph, which shows almost identical curves for the with-control and without-control cases. It gives evidence that u_2^* is a poor control.

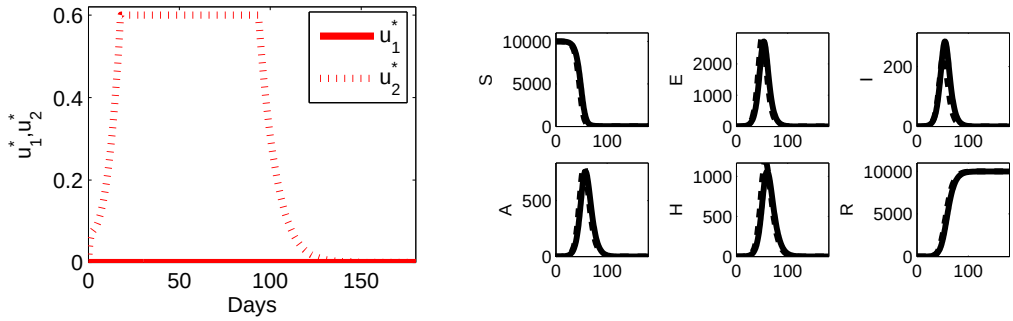

FIGURE 2. The graph on the left shows the optimal control scenario for the hospitalization only case ($u_1^* = 0$ and $0 \leq u_2^* \leq 0.6$). The graphs on the right represents population in each class(S, E, I, A, H, R), where solid lines represent state variables without control and dashed lines represent state variables with control.

In Fig. 3, we considered no hospitalization ($u_2^* = 0$) only intervention ($0 \leq u_1^* \leq 0.6$). The optimal control scenario and the corresponding solution of the state variables are shown in the

graph, which reveals a significant decrease in infected individuals from implementing optimal control. It establishes that u_1^* has the potential to control the disease outbreak.

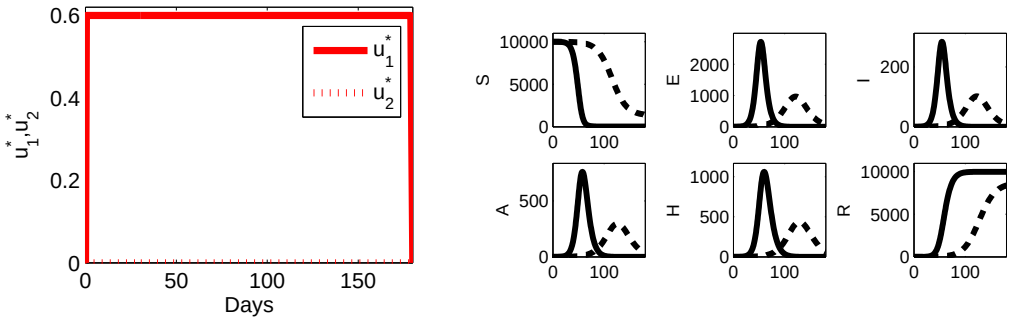

FIGURE 3. The graph on the left shows the optimal control scenario for the prevention-only case ($u_2^* = 0$ and $0 \leq u_1^* \leq 0.6$). The graph on the right represents the population in each class (S, E, I, A, H, R), where solid lines represent state variables without control and dashed lines represent state variables with control.

In Fig. 4, we considered both hospitalization ($0 \leq u_2^* \leq 0.6$) and intervention ($0 \leq u_1^* \leq 0.6$). The optimal control scenario and the corresponding solution of the state variables are shown in the graph which also reveals a significant decrease in infected individuals from implementing optimal control. It establishes that combined implementation of u_1^* and u_2^* could also be planned to control the disease outbreak.

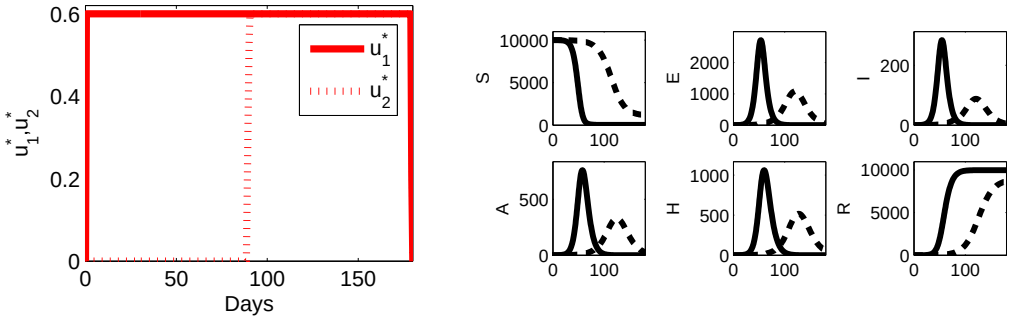

FIGURE 4. The graph on the left shows the optimal control scenario for both prevention ($0 \leq u_1^* \leq 0.6$) and hospitalization ($0 \leq u_2^* \leq 0.6$). The graph on the right represents the population in each class (S, E, I, A, H, R), where solid lines represent state variables without control and dashed lines represent state variables with control.

According to the simulation results, preventing the spread of infection by controlling u_2 only is ineffective. However, the intervention to prevent by only controlling u_1 as well as intervention by both controls u_1 and u_2 is effective.

5. CONCLUSIONS

In this paper, we tried to replicate the 2015 MERS outbreak scenario in South Korea and suggested control strategies to reduce the outbreak. Preventive measures to reduce contact rates and hospitalization are two candidate control measures.

Qualitative analysis of optimal implementation of these two control measures was performed using numerical tools. Our analysis shows, that hospitalization only is not sufficient to reduce the outbreak; rather, preventative efforts alone could reduce the outbreak. That is, hospitalizing infected individuals does not help to prevent the spread of infection after MERS-CoV has occurred. It is more effective for the infected person to avoid contact from outside than to be hospitalized after MERS-CoV occurred. It is worth mentioning that, in practice, self-quarantine for a number of individuals suspected of being exposed to MERS-CoV in the South Korean case had a significant effect in stopping the epidemic.

APPENDIX

A. Basic Reproduction Number $\mathcal{R}_0$.

$$\mathcal{F} = \begin{bmatrix} \beta\frac{(I+l_1A+l_2H)}{N}S \\ 0 \\ 0 \\ 0 \end{bmatrix}, \qquad \mathcal{V} = \begin{bmatrix} \kappa E \\ -\kappa\rho E + (\gamma_a+\gamma_I I) \\ -\kappa(1-\rho)E + \gamma_I A \\ -\gamma_a I + \gamma_r H \end{bmatrix} \tag{5.1}$$

$$F = \begin{bmatrix} 0 & \beta & \beta l_1 & \beta l_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \; V = \begin{bmatrix} \kappa & 0 & 0 & 0 \\ -\kappa\rho & \gamma_a+\gamma_I & 0 & 0 \\ -\kappa(1-\rho) & 0 & \gamma_I & 0 \\ 0 & -\gamma_a & 0 & \gamma_r \end{bmatrix} \tag{5.2}$$

$$FV^{-1} = \begin{bmatrix} \frac{\beta\rho}{\gamma_a+\gamma_I} + \frac{\beta\rho\gamma_a l_2}{\gamma_r(\gamma_a+\gamma_I)} + \frac{\beta(1-\rho)l_1}{\gamma_I} & \frac{\beta}{\gamma_a+\gamma_I} + \frac{\beta\gamma_a l_2}{\gamma_r(\gamma_a+\gamma_I)} & \frac{\beta l_1}{\gamma_r} & \frac{\beta l_2}{\gamma_r} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Then the basic reproduction number, $\mathcal{R}_0$, is calculated from the dominant eigenvalue of FV^{-1}:

$$\begin{aligned} \mathcal{R}_0 &= \beta\frac{\gamma_a\gamma_r l_1 + \gamma_I\gamma_r l_1 + \gamma_I\gamma_r\rho - \gamma_a\gamma_r l_1\rho - \gamma_I\gamma_r l_1\rho + \gamma_a\gamma_I l_2\rho}{\gamma_I\gamma_r(\gamma_a+\gamma_I)} \\ &= \beta\left(\frac{\rho}{\gamma_a+\gamma_I} + \frac{\rho\gamma_a l_2}{\gamma_r(\gamma_a+\gamma_I)} + \frac{(1-\rho)l_1}{\gamma_I}\right). \end{aligned} \tag{5.3}$$

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