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Applying discrete SEIR model to characterizing MERS spread in Korea

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Since the first outbreak of Middle East Respiratory Syndrome (MERS), Korea has a quite rapid MERS spread compared to other countries. Possible causes for such a sudden increase include the undiagnosed initial patient and lapses in infection control practices. To characterize MERS infection and transmission, this paper applies the period-based discrete SEIR model. Infected people of SEIR model shows a good fit to observed patients and MERS will become extinct around 113 days since the first outbreak. Through an effective quarantine plan, if we can reduce exposable people by 20%, it is estimated that the maximum number of infectious people may decrease by about 69% and MERS fade-out period will be shortened by about 30%. Simulations on assumed model support that Korean government's two policies to control MERS infection rate are effective in lessening its spread. Simulation on reproduction ratio scenarios in SEIR model indicates that success in early infection control practices is critical for shortening the period of disease fade-out. Even there are some restrictions and assumptions on SEIR model simulation, our simulation results are to be helpful in developing strategies to prevent the infectious diseases like MERS.

Keywords: MERS in Korea; SEIR model; simulation; MERS control policy.

1. Introduction

Middle East Respiratory Syndrome (MERS) is an illness caused by a corona virus. MERS was first reported in Saudi Arabia in September 2012. So far, most cases of

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MERS have been linked to countries in Middle East. It is known that MERS has spread from ill people to others through close contact, such as caring for or living with an infected person.¹ The clusters detected so far are mostly are small and there have been no reports of strained transmission of MERS within the community. Available data indicate that MERS has not yet readily adapted to infecting human to human transmission.²

Due to its high fatality rate and lack of knowledge regarding its primary source and mode of transmission, MERS becomes major concern of many countries.² Outside the Middle East, the largest known outbreak of MERS occurred in Korea in May 2015. A 68-year-old man who had been traveling through the Middle East returned to Seoul, Korea and promptly developed MERS symptoms. He was diagnosed with the virus on 20 May.³ On 1 July, laboratory confirmed cases of MERS reached 186 persons and the number of death was 33.⁴ In the past, MERS has not spread easily around Middle East countries. Sporadic cases have been imported to Europe, Africa, Asia, and North America via returning travelers from Middle East, but no sustained transmission has been reported in those regions. Compared to previous spread of MERS in those countries, Korea has experienced a rapid spread of MERS and many MERS patients occurred in a short period of time.³

It is not clear whether MERS has the potential of epidemic spread. However, transmission appears limited among family members but may be magnified in health care settings in Saudi Arabia.^{5,6} Investigation on MERS transmission pathway in Korea may reveal similar spread appearances as in Saudi Arabia. Epidemiologists conjecture major causes of such a sudden increase in MERS cases to be the undiagnosed initial patient, lapses in infection control practices, and Korean culture to seek family-care at overcrowded hospitals.³

An understating of the MERS epidemiology and transmission are critically needed to devise effective surveillance, prevention, and control strategies. To assess the transmission potential of epidemic diseases, SEIR model is often applied.^{7–11} In SEIR model, individuals move from being susceptible to exposed (but not yet infectious), and then move to infectious before recovering. Typically in SEIR model, parameters of transition rates from one state to another state are assumed constant through whole period (from onset of disease to its fade-out time). As in Saudi Arabia, most of the MERS cases in Korea occurred in health care facilities, and closing a MERS-linked hospitals or operating MERS-specialized hospitals may tremendously affect the MERS infection rate.⁴ Considering this, we suggest SEIR model with different transmission rate of infection depending on periods rather than a constant rate throughout the whole periods.¹²

Even discrete SEIR model has some limitations on describing the spread of infectious disease,¹³ under assumption that MERS infection rates change for separated periods, we apply the period-based discrete SEIR model to characterize a possible spread of MERS in Korea. We first identify how the MERS was developed into infection through the exposed and characterize MERS infection and transmission from the susceptible population to infected patients. Based on estimated SEIR model, we additionally identify, under some certain assumptions, the effects of the following:

- lowering the population of susceptible individuals
- quarantine of the infected people or education of the public on how to lessen the contacts between infected and susceptible people
- medicine that shortens the symptoms of MERS

to the number of infected people and fade-out period of MERS. Also we investigate the relationship between the number of the infected and the basic reproduction number under certain conditions on translation rates of model.

2. MERS Outbreak in Korea

Since the first occurrence of MERS on 20 May 2015, Korea Centers for Disease Control and Prevention (CDC) continues to report about MERS development in Korea. Table 1 shows daily report on MERS infection including patients laboratory confirmed, recovered or dead from disease, under treatment and quarantine, and released from quarantine from 20 May to 11 October 2015. On 10 July (for less than 60 days since the onset of MERS), 186 individuals were confirmed as MERS-infected cases, among them, 128 are recovered, 36 were dead, 22 patients were still under treatment; 513 were quarantined; and 16,168 were released from quarantine. The confirmed cases are categorized into three groups: inpatients (82 cases, 44%), their family members or visitors to patients (65 cases, 35%), and medical professionals or staffs (39 cases, 21%).⁴ This implies that majority of MERS infections were linked to health care facilities and households or communities of infected cases. Group types of MERS patients in Korea are quite similar to those of Saudi Arabia. which has the largest number of people diagnosed as MERS in the world.^{6,14} The WHO noted that major causes of sudden increase in MERS cases may be lapses in infection control practices and Korean culture to seek family care at overcrowded hospitals.^{3,15}

Careful investigation on MERS data indicates that initial infected patients increased suddenly until Mid-June 2015. Korean government failed to control MERS initially and Korea had so many MERS patients in a short time. After a quick spread, Korean government realized the seriousness of MERS and took two actions to control its spread. Korea CDC publically disclosed MERS-infected information such as MERS-linked hospital names on 7 June, which was the 18th day after the first MERS outbreak, and closed the MERS-linked hospitals on 13 June, which was the 24th day after the MERS onset. Around this time, Korean government better understood the risk of MERS and provided the establishment of public health and clinical infrastructures to control MERS.⁴ As noted earlier, insufficient infection control practices to quarantine the infected people to lessen the contacts between infected and susceptible people may be major causes in a rapid MERS spread in

| Date | LC | RC | D | UT | UQ | RQ | Date | LC | \mathbf{RC} | D | UT | UQ | RQ |
|-------------------|-----|-----|----|-----|------|------------------|--------|-----|---------------|----|----|-----|--------|
| 20 May | 2 | 0 | 0 | 2 | 3 | 0 | 8 Jul | 186 | 120 | 35 | 31 | 689 | 15,886 |
| $21 \mathrm{May}$ | 3 | 0 | 0 | 3 | 64 | 0 | 9 Jul | 186 | 125 | 35 | 26 | 566 | 16,102 |
| 22 May | 3 | 0 | 0 | 3 | 58 | 0 | 10 Jul | 186 | 128 | 36 | 22 | 513 | 16,168 |
| 23 May | 3 | 0 | 0 | 3 | 61 | 0 | 11 Jul | 186 | 130 | 36 | 20 | 485 | 16,197 |
| 24 May | 3 | 0 | 0 | 3 | 62 | 0 | 12 Jul | 186 | 130 | 36 | 20 | 451 | 16,231 |
| 25 May | 3 | 0 | 0 | 3 | 62 | 0 | 13 Jul | 186 | 131 | 36 | 19 | 410 | 16,278 |
| 26 May | 5 | 0 | 0 | 5 | 61 | 0 | 14 Jul | 186 | 132 | 36 | 18 | 322 | 16,368 |
| 27 May | 5 | 0 | 0 | 5 | 120 | 0 | 15 Jul | 186 | 133 | 36 | 17 | 258 | 16,432 |
| 28 May | 7 | 0 | 0 | 7 | 127 | 0 | 16 Jul | 186 | 134 | 36 | 16 | 155 | 16,538 |
| 29 May | 13 | 0 | 0 | 13 | 129 | 0 | 17 Jul | 186 | 135 | 36 | 15 | 98 | 16,595 |
| 30 May | 15 | 0 | 0 | 15 | 462 | 6 | 18 Jul | 186 | 136 | 36 | 14 | 68 | 16,625 |
| 31 May | 18 | 0 | 0 | 18 | 715 | 8 | 19 Jul | 186 | 136 | 36 | 14 | 22 | 16,671 |
| 1 Jun | 25 | 0 | 1 | 24 | 789 | 33 | 20 Jul | 186 | 136 | 36 | 14 | 5 | 16,688 |
| 2 Jun | 30 | 0 | 1 | 29 | 1364 | 52 | 21 Jul | 186 | 137 | 36 | 13 | 3 | 16,690 |
| 3 Jun | 30 | 0 | 3 | 27 | 1667 | 62 | 22 Jul | 186 | 138 | 36 | 12 | 3 | 16,690 |
| 4 Jun | 36 | 0 | 4 | 32 | 1820 | 221 | 23 Jul | 186 | 138 | 36 | 12 | 1 | 16,692 |
| 5 Jun | 42 | 1 | 5 | 36 | 1866 | 386 | 24 Jul | 186 | 138 | 36 | 12 | 1 | 16,692 |
| 6 Jun | 64 | 1 | 5 | 58 | 2361 | 560 | 25 Jul | 186 | 138 | 36 | 12 | 1 | 16,692 |
| 7 Jun | 87 | 1 | 5 | 81 | 2508 | 583 | 26 Jul | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 8 Jun | 95 | 2 | 7 | 86 | 2892 | 607 | 27 Jul | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 9 Jun | 108 | 3 | 7 | 98 | 3439 | 641 | 28 Jul | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 10 Jun | 122 | 4 | 9 | 109 | 3805 | 955 | 29 Jul | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 11 Jun | 126 | 7 | 10 | 109 | 3680 | 1249 | 30 Jul | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 12 Jun | 138 | 9 | 13 | 116 | 4014 | 1930 | 31 Jul | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 13 Jun | 145 | 10 | 14 | 121 | 4856 | 2473 | 1 Aug | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 14 Jun | 150 | 14 | 16 | 120 | 5216 | 3122 | 2 Aug | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 15 Jun | 154 | 17 | 19 | 118 | 5586 | 3505 | 3 Aug | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 16 Jun | 162 | 19 | 19 | 124 | 6508 | 3951 | 4 Aug | 186 | 138 | 36 | 12 | 0 | 16,693 |
| 17 Jun | 165 | 24 | 23 | 118 | 6729 | 4492 | 5 Aug | 186 | 138 | 36 | 12 | 0 | 16.693 |
| 18 Jun | 166 | 30 | 24 | 112 | 5930 | 5535 | 6 Aug | 186 | 139 | 36 | 11 | 0 | 16.693 |
| 19 Jun | 166 | 36 | 24 | 106 | 5197 | 7451 | 7 Aug | 186 | 140 | 36 | 10 | 0 | 16.693 |
| 20 Jun | 169 | 43 | 25 | 101 | 4035 | 8812 | 8 Aug | 186 | 140 | 36 | 10 | 0 | 16.693 |
| 21 Jun | 172 | 50 | 27 | 95 | 3833 | 9331 | 9 Aug | 186 | 140 | 36 | 10 | 0 | 16.693 |
| 22 Jun | 175 | 54 | 27 | 94 | 2805 | 10.718 | 10 Aug | 186 | 140 | 36 | 10 | 0 | 16.693 |
| 23 Jun | 179 | 67 | 27 | 85 | 3103 | 11.210 | 11 Aug | 186 | 140 | 36 | 10 | 0 | 16.693 |
| 24 Jun | 180 | 74 | 29 | 77 | 2642 | 11.936 | 12 Aug | 186 | 140 | 36 | 10 | 0 | 16.693 |
| 25 Jun | 181 | 81 | 31 | 69 | 2931 | 12.203 | 13 Aug | 186 | 140 | 36 | 10 | Õ | 16.693 |
| 26 Jun | 182 | 90 | 31 | 61 | 2467 | 12.958 | 14 Aug | 186 | 140 | 36 | 10 | Ő | 16.693 |
| 27 Jun | 182 | 91 | 32 | 59 | 2562 | 13.008 | 15 Aug | 186 | 140 | 36 | 10 | Ő | 16.693 |
| 28 Jun | 182 | 93 | 32 | 57 | 2682 | 13,136 | 16 Aug | 186 | 140 | 36 | 10 | Ő | 16,693 |
| 29 Jun | 182 | 95 | 33 | 54 | 2638 | 13,354 | 17 Aug | 186 | 140 | 36 | 10 | Ő | 16 693 |
| 30 Jun | 182 | 97 | 33 | 52 | 2451 | 13,554 | 18 Aug | 186 | 140 | 36 | 10 | Ő | 16 693 |
| 1 Jul | 183 | 102 | 33 | 48 | 2101 | 13 821 | 10 Aug | 186 | 140 | 36 | 10 | 0 | 16 693 |
| 2 Jul | 184 | 102 | 33 | 42 | 2067 | 10,021 14.062 | 20 Aug | 186 | 140 | 36 | 10 | 0 | 16 693 |
| 2 Jul | 185 | 111 | 33 | 41 | 1434 | 14702 | 21 Aug | 186 | 140 | 36 | 10 | 0 | 16 693 |
| 4 Jul | 186 | 116 | 33 | 37 | 982 | 15 158 | 22 Aug | 186 | 140 | 36 | 10 | 0 | 16 693 |
| 5 Jul | 186 | 117 | 33 | 36 | 907 | 15 410 | 22 Aug | 186 | 140 | 36 | 10 | 0 | 16 603 |
| 6 Jul | 186 | 118 | 33 | 35 | 674 | 15 669 | 20 Aug | 186 | 140 | 36 | 10 | 0 | 16 603 |
| 7 Jul | 186 | 119 | 34 | 33 | 811 | 15,761 | 25 Aug | 186 | 140 | 36 | 10 | 0 | 16.693 |
| | | | | | | | | | | | | ~ ~ | |

Table 1. MERS cases in Korea.⁴

Note: LC: Laboratory-Confirmed, RC: Recovered, D: Dead, UT: Under Treatment, UQ: Under Quarantine, RQ: Released from Quarantine.

| Date | LC | \mathbf{RC} | D | UT | UQ | RQ | Date | LC | RC | D | UT | UQ | RQ |
|-------------------|-----|---------------|----|----|----|------------|-------------------|-----|-----|----|----|----|------------|
| 26 Aug | 186 | 140 | 36 | 10 | 0 | 16,693 | 19 Sep | 186 | 143 | 36 | 7 | 0 | 16,693 |
| $27 \mathrm{Aug}$ | 186 | 140 | 36 | 10 | 0 | $16,\!693$ | 20 Sep | 186 | 144 | 36 | 6 | 0 | $16,\!693$ |
| 28 Aug | 186 | 140 | 36 | 10 | 0 | 16,693 | $21 \mathrm{Sep}$ | 186 | 144 | 36 | 6 | 0 | 16,693 |
| 29 Aug | 186 | 141 | 36 | 9 | 0 | 16,693 | 22 Sep | 186 | 144 | 36 | 6 | 0 | 16,693 |
| 30 Aug | 186 | 141 | 36 | 9 | 0 | $16,\!693$ | $23 \mathrm{Sep}$ | 186 | 144 | 36 | 6 | 0 | $16,\!693$ |
| 31 Aug | 186 | 141 | 36 | 9 | 0 | 16,693 | $24 \mathrm{Sep}$ | 186 | 144 | 36 | 6 | 0 | 16,693 |
| $1 \mathrm{Sep}$ | 186 | 141 | 36 | 9 | 0 | $16,\!693$ | $25 { m Sep}$ | 186 | 144 | 36 | 6 | 0 | $16,\!693$ |
| 2 Sep | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | 26 Sep | 186 | 144 | 36 | 6 | 0 | 16,693 |
| 3 Sep | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | $27 \mathrm{Sep}$ | 186 | 144 | 36 | 6 | 0 | $16,\!693$ |
| $4 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | 28 Sep | 186 | 144 | 36 | 6 | 0 | 16,693 |
| 5 Sep | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | $29 \mathrm{Sep}$ | 186 | 144 | 36 | 6 | 0 | 16,693 |
| 6 Sep | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | $30 { m Sep}$ | 186 | 144 | 36 | 6 | 0 | 16,693 |
| $7 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | 16,693 | 1 Oct | 186 | 145 | 36 | 5 | 0 | 16,693 |
| $8 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | 16,693 | 2 Oct | 186 | 145 | 36 | 5 | 0 | 16,693 |
| $9 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | 16,693 | 3 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| $10 { m Sep}$ | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | 4 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| $11 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | 5 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| $12 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | 6 Oct | 186 | 145 | 36 | 4 | 0 | 16,693 |
| $13 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | $16,\!693$ | 7 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| $14 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | 16,693 | 8 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| $15 \mathrm{Sep}$ | 186 | 142 | 36 | 8 | 0 | 16,693 | 9 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| 16 Sep | 186 | 142 | 36 | 8 | 0 | 16,693 | 10 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| 17 Sep | 186 | 142 | 36 | 8 | 0 | 16,693 | 11 Oct | 186 | 146 | 36 | 4 | 0 | 16,693 |
| $18 \mathrm{Sep}$ | 186 | 143 | 36 | 7 | 0 | $16,\!693$ | | | | | | | |

Table 1. (Continued)

Korea. Regarding this point, we intend to investigate effects of control practices to lower the MERS spread through simulation on SEIR model.

3. Discrete SEIR Model for MERS Spread

It is assumed that MERS is a disease that follows a classic mathematical model known as discrete SEIR model given in Fig. 1.^{8,10} Similar to the original SEIR model, we divide the population into susceptible (S), exposed (E), infected (I), and recovered or dead (R) individuals. By interacting with infectious individual, individual moves from the susceptible state S to the exposed state E with transmission rate β . MERS is known to have an incubation period between exposure to the pathogen and the development of clinical symptoms.⁶ During incubation period, exposed individual is not infectious. After incubation period, exposed individual transits from the state E to the state I at a rate ϵ , which reflects the incubation rate of the MERS. Once a person has an infection of MERS, that individual either develops immunity to prevent reinfection of MERS or is dead due to MERS illness with a rate of γ .

In the given model, α represents the immunity loss rate, and μ and μ^* are natural death and birth rates, respectively. This study assumes that the immunity loss rate α is zero since individual recovered from MERS would show long lasting



Fig. 1. SEIR compartment model.

immunity or individual would be dead from MERS. Also we ignore the rates of birth (μ^*) and death (μ) in the model because the considered time interval is not sufficiently long.¹⁰

As shown in Fig. 1, SEIR model has four compartments or states, and therefore four equations are required to parameterize it. Individual moves from the susceptible state S to the exposed state E by interacting with infectious people. There can be no new infection if there are no susceptible people left to infect. Therefore, the rate of change in the number of exposed people is proportional to $\beta I * S/N$, where N is the total population considered. The number of exposed people over time includes exposed people in the past and people newly exposed to the disease, and decrease by the number of people moved to the state I. Infected people transit from the Istate to the state R at a rate γ . Based on above discussion, the number of change in each state for a unit time interval of t (one day) is then:

$$S_{t+1} = S_t - \beta I_t * S_t / N, \tag{1}$$

$$E_{t+1} = E_t + \beta I_t * S_t / N - \epsilon E_t, \tag{2}$$

$$I_{t+1} = I_t + \epsilon E_t - \gamma I_t, \tag{3}$$

$$R_{t+1} = R_t + \gamma I_t. \tag{4}$$

(For more detailed discussion of above equations, see Refs. 8 and 10.)

Equations (1)–(4) include finite difference equations that predict change in the number of people in each state over a finite step of time. Using these equations, with the total population N, the parameters of β , ϵ , and γ , and the initial numbers of S, E, I, and R states, we can derive the numbers of individuals at states S, E, I, and R over the time t.

People are moving the state S > E > I > R as the infection of disease acts, and after some steps of k, the disease becomes extinct, which results in $I_k = 0$. Using simulation on the SEIR model, we will characterize how the MERS spreads within the confines of assumed population. We find the best parameters of β , ϵ , and γ which yield the least sum of square errors (LSSE) between the observation on the infected (CDC data on the infected) and the SEIR model estimate of I_t .

In general, the SEIR model assumes that constant values of parameters throughout simulation period. But in this study, we suppose that the transmission rate β moving from the state S to the state E could change at a certain time due to actions affecting the contact ratio of individual in state S with infected people. When a large amount of change in the transmission rate β occurs, from this instant, it would be better to apply another SEIR model with different parameters for describing the transmission of infection system. Thus we utilize the period-based simulation where the SEIR model could have different values of β for separated periods.

To understand a type of possible spread of MERS, we often infer the basic reproduction number, R_0 which is given by

$$R_0 = \beta / \gamma. \tag{5}$$

This number provides a useful metric for assessing the transmission potential of an emerging pathogen such as MERS.¹⁶ Based on an estimated SEIR model, we investigate spreads of MERS for several different values of reproduction numbers.

4. Simulation on SEIR Model

SEIR model above is a discrete dynamical system, where populations are examined at discrete time steps. In a finite difference equation, we set the time step t fixed as one day and the value at the current time step is used to predict the value for the next step. We consider that MERS acts over a very short period of time, thus we will simplify our model by assigning that the population remains constant with size of N.

Considered model also assumes that the population is well mixed, so all individuals are equally likely to encounter other individuals. It is known that SEIR model probably works well for local populations such as specific schools.⁶ Korea CDC reported that the vast majority of MERS patients in Korea had potential exposure to other people mostly in health care facilities.⁴ Even when there are significant regional outbreaks, often containing regional outbreaks is a key to controlling a disease.⁷ Thus in this study, we confine the number initially susceptible people only to the people quarantined due to contacts with infectious patients rather than entire society of Korea. SEIR model with above assumptions does not account for many factors that could prove important in the course of the disease, yet it gives some understanding how MERS spreads in a short period of time and what might affect its spread.

At time step t (day), population N satisfies $N = S_t + E_t + I_t + R_t$ for SEIR model. Therefore we have to keep track of individuals classed as states as simulation continues. We simulate the SEIR model and try to fit it to the MERS data (infected individuals) in Table 1. We assume that the control population N consists of the infected, the recovered and dead from MERS, the quarantined, and the released from quarantine individuals that Korea CDC reported (see data on 25 July in Table 1). So the number of N is assumed to be 16,883. This is obviously not representative of a well-mixed homogeneous population. However, it is very difficult to obtain a good choice for N. With this assumption for our population, it becomes natural to take $S_0 = 16,878$, $E_0 = 3$, $I_0 = 2$, $R_0 = 0$ at time 0. Simulation on SEIR model will determine the best values of the parameters β , ϵ , and γ that fit the infected individuals in Table 1. These parameters are a key to understanding the nature of a disease. Up to date, we have little information concerning the exposed individuals.² The general SEIR model assumes the values of parameters remain same during whole periods of interest. However in this study, we assume values of SEIR model parameters before a specific event of time t_p could be considerably different from those after time of t_p . Thus one SEIR model is used to fit the infected data for periods before t_p and another SEIR model with different parameters is used to fit the infected data for periods after t_p .

About 20 days later after first outbreak of MERS, Korean government realized the seriousness of MERS spread, and then enforced two actions to control the MERS spread. We consider that the exposed rate would be quite lessened according to government actions of publicly disclosing MERS-linked-hospital names on 7 June, 2015, closing such hospitals and operating specialized hospitals for MERS on 13 June, 2015. Such actions may promptly induce reduced contacts with infectious people and result in lowering the exposure rate as well as infection rate.

Based on these conjectures, we separate the whole simulation periods into three parts of periods according to government actions: the first part begins from 20 May to 7 June (at time of T1), the second one is from 8 June to 13 June (at time of T2), and the third one is from 14 June to the end of simulation run. The second part simulation on SEIR model starts at T1 and its starting values of S, E, I, and R are those generated from the first part simulation ended at T1. In the same way, the third part simulation on SEIR model starts at T2 with values of S, E, I, and R of simulation output ended at T2 as an initial condition.

5. Simulation Results

We perform simulation for three different excusive periods. The Period 1 consists of 19 days (20 May–7 June 2015), the Period 2 consists of 6 days (8 June–13 June 2015), and the Period 3 contains 120 days (13 June–11 October 2015). Using the statistical program \mathbb{R}^{17} we obtain the LSSE for infected patients, and best model parameters of β , ϵ , and γ that match them. Table 2 presents estimated parameters of SEIR models for three different exclusive periods.

The transition rate β decreases as simulation period increases, it is 2.0 for Period 1, 1.1 for Period 2, and 0.5 for Period 3, respectively. From this result, we note that government's two actions to control the spread of MERS are effective in reducing the transition rate from susceptible individual to exposed individual. On the other hand, the incubation rate ϵ remains same for three periods, and the recovery rate γ increases a little from 0.6 to 0.7 as simulation time increases. The coefficient of determination, R^2 is 98.5%, which provides the measure of fit of SEIR model to infected people. This result implies that SEIR model well explains the variation of infected patients for whole periods.

| Parameters | Period 1 | Period 2 | Period 3 |
|------------|----------|----------|----------|
| β | 2.0 | 1.1 | 0.5 |
| ϵ | 0.2 | 0.2 | 0.2 |
| γ | 0.6 | 0.7 | 0.7 |
| LSSE | 298 | 123 | 4079 |
| R^2 | | 98.5% | |
| p-value | | 0.000 | |

Table 2. Estimated parameters.

The basic reproduction ratio, β/γ provides a measure of how rapidly MERS will spread and how much of the population will be affected by a particular disease.¹⁰ The values of reproduction ratios for three periods are 3.33, 1.57, and 0.71, respectively. Higher ratio induces a more rapid spread of disease and lower ratio lessens the speed of spread. When this ratio is greater than 1, the disease is infectious, but when this ratio is less than 1, the disease will die out.¹⁶ In the situation that a medicine for curing MERS yet has not been developed, by implementing interventions that lower the transmission rate, we can reduce the reproduction ratio.

Figure 2 presents the fitted graphs of infected patients and exposed people by SEIR model, and infected observations in Table 1. Fitted curve for infected people presents similar pattern of observed patients and MERS will be extinct around 113 days after the first outbreak.

In terms of SEIR model, increases or decreases of S_0 , β , and γ affect the spread of MERS. Developed vaccine will reduce the initial number of susceptible population. Suppose that S_0 decreases by 5%. We resimulate the SEIR model with initial condition that $S_0 = 0.95N - I_0 - E_0$ and the same values of β , ϵ , and γ as given in an estimated model. Secondly we consider a certain treatment that can reduce the contact rate of individual with MERS patients. This treatment results in lowering



Fig. 2. Infected observations and SEIR estimation.



Fig. 3. MERS control scenarios in SEIR model.

the value of β in SEIR model. Suppose we lower this value by 5% with no other changes in SEIR model except new β . Finally we suppose the medicine for MERS is developed. This will induce an increase of γ in SEIR model. Without any changes in other parameters, suppose we increase this value only by 5%.

To investigate these three treatments effects on the number infected patients, we independently simulate SEIR model. Figure 3 shows how three different treatments affect the numbers of infected people as the time step t increases. Three treatments significantly lessen the spread of MERS, and the effects of developed medicine and reduction in contact are similar.

Among considered three treatments, either medical vaccine or medicine is not yet developed. So the possible treatment to control the spread of a new disease like MERS would be preventive measure of quarantining with pathogen. With respect to this point, we analyze how the second treatment of reducing the value of β affects MERS spread. We decrease the values of β by 5%, 10%, and 20%, respectively. Significant reductions in infected people are observed in Fig. 4. For instance, 20%



Fig. 4. Contact reduction scenarios in SEIR model.



Fig. 5. Reproduction ratio scenarios in SEIR model.

reduction in β leads to reduction of infected people by about 69% and MERS fade-out period is shortened by about 30%.

Failure to initial control over MERS is one of the major reasons why Korea has so many MERS patients in a short period of times since the first outbreak.³ If MERS would be well controlled initially, then its spread may be quite different from observed one. We develop simulation scenarios in terms of reproduction ratios and estimate new patterns of MERS spread when the values of R_0 in Eq. (5) are given by 0.7, 0.9, and 1.1. In Table 2, the estimated parameters of ϵ and γ are about 0.2 and 0.7, respectively and quite stable for three periods. So we assume that a new scenario-based simulation may yield similar estimations for parameters of ϵ and γ . With this assumption and given three values of the R_0 , we run simulation and estimate the number of infected patients and guess when the disease will fade out. Figure 5 presents the number of the infected patients for three values of the reproduction rate. When this rate is either 0.7 or 0.9 (less than 1.0), there seems to be no increase in infected patients and disease will fade out soon. Note that in Table 2, the value of R_0 dropped from 3.3 (for the first period) to 0.7 (23 days later after onset of MERS). So success in early infection control practices would yield a spread patterns of $R_0 = 0.7$ (or 0.9) in Fig. 5.

6. Discussion

Many epidemiologists are concerned how Korea MERS outbreak is so big in a short period. The WHO notes that a rapid spread of MERS in Korea may be caused by failure to fast quarantine of infected people from susceptible people. To understand the spread of MERS in Korea, we apply the discrete SEIR model and characterize the possible spread of MERS from its first outbreak to official end. In the course of simulation on SEIR model, we separate the whole periods into three disjointed parts of periods according to government actions which may affect the infection rate of disease.

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The determination coefficient of assumed model is more than 0.98 and estimated curve of infected people shows a very good fit to observed patients. Simulation results suggest that MERS in Korea will become extinct around 113 days after the first outbreak. Three treatments controlling MERS spread are effective in reducing number of patients and shortening the fade-out period of MERS. Under the situation that medical vaccine or medicine is not developed, quarantining infected people from susceptible people is an effective way to control MERS spread. 20% reduction of exposable people through an effective quarantine plan may decrease the maximum number of infectious people by about 69% and MERS fade-out period may be shortened by about 30%. Assumed simulations based on several scenarios suggest that disclosing MERS linked-hospitals and operating specialized MERS hospitals are very helpful in reducing the spread of MERS in Korea. Reproduction Ratio Scenarios in SEIR model imply that success in early infection control practices is critical for a short period of disease fade-out.

Even SEIR model has some restrictions in describing the disease spread like MERS and there are some assumed conditions in simulation of SEIR model, our simulation results help to understand how MERS spreads in Korea and how we can control the epidemic disease like MERS in the future. We hope this research will be helpful in developing strategies to prevent infectious diseases like MERS.

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