Evaluation of the basic reproduction number of MERS-CoV during the 2015 Outbreak in South Korea*

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Abstract: In 2015 an outbreak of Middle East Respiratory Syndrome (MERS) has occurred in South Korea, which has been known to be the second biggest outbreak of MERS so far. In this paper we study an estimation of the basic reproduction number of the coronavirus (CoV) of MERS based on the reported data from the MERS spread in South Korea. To this end we employ a mathematical model described by a set of ordinary differential equations, *i.e.* the well-known susceptible-infected-removed (SIR) model. First we fit the model to the epidemic curve data obtained from the outbreak. Then we can identify the model parameters and also the basic reproduction number. Note that there had been no control intervention during the early stage of the MERS outbreak in South Korea, which can be considered as the best condition for the estimation study of intrinsic epidemic parameters of MERS, such as basic reproduction number.

Keywords: SIR model, MERS-CoV, Basic reproduction number.

1. INTRODUCTION

A novel coronavirus, the Middle East respiratory syndrome-coronavirus (MERS-CoV), causes the MERS. In 2012 the first case of this viral respiratory disease was identified in Saudi Arabia [17]. After the first MERS case in South Korea was reported on 20 May 2015, a large outbreak of MERS occurred in the Republic of Korea from May 2015 to July 2015.

This outbreak in South Korea has known to be the second largest MERS outbreak [13]. Due to the outbreak, 36 infected patients have died, 186 infection cases have been confirmed, and at least total 16,693 suspicious people have been isolated in South Korea [14]. In this paper, particularly based on the reported data of the case of 2015 outbreak in South Korea, we study an estimation of the basic reproduction number of the MERS-CoV.

Basic reproduction number, which is usually denoted as R_0, of an infection disease is considered as the number of secondary cases which one infected primary subject produces on average in an uninfected and totally susceptible population, over the infectious period [2,6,7,10–12, 15]. Thus it also means an estimation of the growth of the corresponding epidemic at the beginning of the outbreak, assuming that all subject in the total population is susceptible. In some literature R_0 is also referred as basic reproductive (or reproduction) number (or ratio). Note that basic reproductive (or reproduction) rate is not correct because R_0 is a number without dimension and does not correspond to any physical quantity related to 'rate'.

The basic reproduction number of an infectious disease is an useful metric when we determine whether the disease will spread or not [8]. This is because R_0 pro-

vides an estimation of the growth rate at the beginning of the disease outbreak when most individuals are susceptible [5].

We estimate the basic reproduction number of a disease mainly because of the following two reasons [12]: first, R_0 can be used to evaluate the risk of the corresponding infectious disease in a relative sense, and accordingly to compare the infectivity of the disease with the infectivity of other familiar diseases. Second, we can evaluate R_0 two times, before and after a control measure is intervened, in order to determine how we apply the control intervention such that the reproduction number is reduced less than 1.

Note that, to be distinguished with basic reproductive number, this reproduction number with an implementation of control intervention is referred as effective production number, R_{eff}. Consequently the efficacy of a control intervention is generally evaluated quantitatively by R_{eff}. The case with $R_{\text{eff}} < 1$ implies a successful intervention so that we control the disease outbreak ultimately by reducing the reproduction number below the threshold.

To evaluate the reproduction number of the MERS-CoV based on the data of 2015 MERS outbreak in South Korea, we employ a mathematical model described by a set of ordinary differential equations (ODEs), *i.e.* the well-known susceptible-infected-removed (SIR) model [3, 8, 16]. Using the reported data from the MERS outbreak in South Korea we can estimate the basic reproductive number of MERS-CoV.

First we fit the considered model to curve data obtained from the epidemic case in South Korea. By model fitting we estimate the model parameters, and then we can estimate R_0. Note that, due to the limited availability of the epidemic data, models which are usually employed

for such a purpose are non-structured deterministic [12].

Although we can find some literature related to the R_0 of MERS-CoV (see [5, 9], for example), we should emphasise that the MERS outbreak situation in South Korea is quite unique because the disease did spread almost freely with no control intervention at all particularly in the early stage of the outbreak.

Note that in the early phage the responses of the Korean government were not properly coordinated [13]. For example even the list of the affected medical facilities in South Korea was not announced publicly during the initial stage. Also note that such a situation can provide optimal opportunity to fit the model to the real epidemic data and thus to study intrinsic properties of the MERS-CoV such as R_0.

The rest of the paper is organised as follows. In Section 2.we introduce an estimation method for the basic reproductive number based on a mathematical model, the set of ordinary differential equations. Then Section 3. presents the estimation result as well as further discussions. Finally the paper is concluded with some future research directions in Section 4.

2. METHOD

In this section we introduce the methodology used in the paper, such as the description of the SIR model.

2.1 SIR model

Nonlinear compartmental models have been developed to study the spread of infectious diseases. Among them, in this paper we employ the SIR model which is given by

$$
\begin{aligned}
\dot{S} &= -\beta SI, \\
\dot{I} &= \beta SI - \nu I, \\
\dot{R} &= \nu I,
\end{aligned}
\tag{1}
$$

where β and ν are the disease transmission rate and the removed rate, respectively. Note that $\beta > 0$ and $\nu > 0$. The states S, I, and R denote the numbers of susceptible, infected, and removed, respectively. Note that the state R corresponds to the sum of the deceased patients and the recovered patients. In each group of S, I, and R subjects, the status of states (*e.g.* susceptibility, infectiveness, etc) is assumed to be homogeneous.

The notation of (1) follows the usage in [16]. The descriptions of the state variables and the system parameters for model (1) is summarised in Table 1. Note that κ and τ in Table 1 will be mentioned in Section 3. For more detailed explanation of the model see, for example, [3, 8, 16].

The model (1) does not includes any term describing birth and death (not caused by the considered infection disease, MERS) in the population. This is because in SIR model for an epidemic it is assumed that the dynamics of infection and recovery is much faster than the progress

Table 1 Descriptions of the state variables and system parameters of the SIR model (1)

State variables and parameters	Descriptions
S	number of susceptible subjects
I	number of infected subjects
R	number of removed subjects
β	disease transmission rate
ν	removed rate
τ	transmissibility of the infection
κ	number of transmittable contacts by infected patient per unit time

of birth and death. Thus epidemic SIR models such as model (1) do not have birth and death dynamics due to the assumption of no net change by births and deaths in the population. When a disease with relatively slow dynamics (for example, an endemic disease) is modelled, the dynamic terms for birth and death must be considered.

For model (1) it is assumed that the system parameters (*i.e.* all rates) are positive constant. Then, by definition of R_0, we have an alternative description of R_0 for model (1):

$$
R_0 = \kappa \tau d,
\tag{2}
$$

where κ is the number of transmittable contacts by each infected patient per unit time, τ is the *transmissibility* of the infection, *i.e.* the probability of infection per contact between susceptible subject and infected subject, and d is the duration of infection.

Note that with the assumption of constant rates in model (1) the duration of infection is the reciprocal number of the removed rate:

$$
d = \frac{1}{\nu}.
$$

3. RESULT

Table 2 shows the status history of the MERS-CoV spread, which have been officially announced by Ministry of Health and Welfare, Korea. The numbers in the 'Infected', 'Deceased', and 'Recovered' columns of the table count the accumulated infected patients, the total dead individuals, and the total individuals back to healthy state, respectively, up to the 'Date'. Note that the removed patients and the recovered patients are also included in the infected patients.

We now denote the total population size by $N(t)$:

$$
N(t) := S(t) + I(t) + R(t).
$$

Table 2 Accumulated MERS-CoV patients in Korea, 2015 [14]

Date	Infected	Deceased	Recovered
20 May	2	0	0
21 May	3	0	0
26 May	5	0	0
28 May	7	0	0
29 May	13	0	0
30 May	15	0	0
31 May	18	0	0
1 June	24	1	0
2 June	25	2	0
3 June	30	2	0
4 June	36	3	0
5 June	42	4	0
6 June	50	4	1
7 June	64	5	1
8 June	87	6	2
9 June	95	7	3
10 June	108	9	4

Then we can see that

$$\dot{N}(t) = \dot{S}(t) + \dot{I}(t) + \dot{R}(t)$$
$$= 0$$

by the summation of the left-hand sides of the equations of model (1). Therefore $N(t)$ must remain a constant for model (1), *i.e.* $N(t) = N(0) := N$. Note that we can reduce the order of model (1) by constant N. For example we can denote the state $S(t)$ by $N - I(t) - R(t)$, resulting in a 2-dimensional model instaed of 3-dimentioanl model (1).

Considering the order of the numbers in Table 2 we assume that

$$N \cong S. \tag{3}$$

This assumption is reasonable since the case number of outbreak is significantly small compared to the size of total population: it is now known that N of South Korea is over 51 millions. Note that we do not need to know the exact number of N for the estimation of the system parameters of model (1), if the case number of outbreak is considerably small compared to the total size of population [1, 4].

Note that

$$\beta = \frac{\kappa\tau}{N},$$

where κ and τ are the number of transmittable contacts by each infected patient per unit time and the transmissibility of the infection, respectively [16].

Thus we now have the following reduced model by assumption (3):

$$\dot{I} = \kappa\tau I - \nu I,$$
$$\dot{R} = \nu I. \tag{4}$$

As indicated in the table the initial condition for the model is given by

$$[I(0), R(0)] = [2, 0].$$

The system parameters are estimated from the data by trial and error, $\kappa\tau = 0.208$ and $\nu = 0.021$.

From the SIR model the *basic reproductive number* is defined in Section 2(Also see [16]):

$$R_0 = \frac{\kappa\tau}{\nu}.$$

Accordingly R_0 of MERS-CoV is determined as 9.9048 (=0.208/0.021).

4. DISCUSSION

This paper has presented an estimation study of the basic reproduction number of MERS-CoV based on the reported data from the 2015 MERS outbreak in South Korea. For this purpose we have used a mathematical deterministic model, *i.e.* the SIR model. Firstly we have fitted the SIR model to the curve data of the epidemic report from the MERS outbreak in South Korea. Then we have identified the model parameters and the basic reproduction number as well.

Since there was not any control intervention at all in the early stage of the MERS outbreak in South Korea, the epidemic case considered in this paper can provide the best condition for the estimation study of some epidemic parameters of MERS, including the basic reproduction number. Usually an estimation of R_0 based on reported epidemic data might be problematic in case that stochastic fluctuations exist in the early stage of the infection spread, or in case that the reporting is not accurate so as to bias the data [12]. Nevertheless the research of this paper is irrelevant to such problematic cases since we have employed the data precisely investigated and reported by [14].

REFERENCES

[1] C.L. Althaus. Estimating the reproduction number of ebola virus (EBOV) during the 2014 outbreak in west africa. *PLOS Currents Outbreaks*, 2014.

[2] R.M. Anderson and R.M. May. *Infectious Diseases of Humans: Dynamics and Control*. Oxfor University Press, 1992.

[3] Roy M. Anderson. Discussion: The Kermack-McKendrick epidemic threshold theorem. *Bulletin of Mathematical Biology*, 53(1-2):1–32, 1991.

[4] G. Chowell, N.W. Hengartner, C. Castillo-Chavez, P.W. Fenimore, and J.M. Hyman. The basic reproductive number of Ebola and the effects of public

health measures: the cases of Congo and Uganda. *Journal of Theoretical Biology*, 229(1):119 – 126, 2004.

[5] Gerardo Chowell, Seth Blumberg, Lone Simonsen, Mark A. Miller, and Ccile Viboud. Synthesizing data and models for the spread of MERS-CoV, 2013: Key role of index cases and hospital transmission. *Epidemics*, 9:40 – 51, 2014.

[6] O. Diekmann and J.A.P. Heesterbeek. *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation*. Wiley, 2000.

[7] O. Diekmann, J.A.P. Heesterbeek, and J.A.J. Metz. On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology*, 28(4):365–382, 1990.

[8] Joseph DiStefano III. *Dynamic Systems Biology Modeling and Simulation*. Academic Press, 2015.

[9] Keisuke Ejima, Kazuyuki Aihara, and Hiroshi Nishiura. Probabilistic differential diagnosis of middle east respiratory syndrome (MERS) using the time from immigration to illness onset among imported cases. *Journal of Theoretical Biology*, 346:47 – 53, 2014.

[10] J.A.P. Heesterbeek. A brief history of R_0 and a recipe for its calculation. *Acta Biotheoretica*, 50(3):189–204, 2002.

[11] J.A.P. Heesterbeek and K. Dietz. The concept of R_0 in epidemic theory. *Statistica Neerlandica*, 50(1):89–110, 1996.

[12] J.M Heffernan, R.J Smith, and L.M Wahl. Perspectives on the basic reproductive ratio. *Journal of The Royal Society Interface*, 2(4):281–293, 2005.

[13] M.H. Hyun and Y. Park. Re: Why the panic? South Korea's MERS response questioned. *BMJ*, 350, 2015.

[14] Korea Hospital Association. *2015 MERS, White paper by Korea Hospital Association*. Korea Hospital Association, 2015.

[15] P. van den Driessche and James Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(12):29 – 48, 2002.

[16] Howard Weiss. The SIR model and the foundations of public health. *MATerials MATemàtics*, 3(17):1–17, 2013.

[17] World Health Organization. Fact sheet 401: Middle east respiratory syndrome coronavirus (MERS-CoV). 2015.