Article

A Simulation on Potential Secondary Spread of Novel Coronavirus in an Exported Country Using a Stochastic Epidemic SEIR Model

Kentaro Iwata [1,*] and Chisato Miyakoshi [2]

[1] Division of Infectious Diseases, Kobe University Hospital; kentaroiwata1969@gmail.com
[2] Department of Research Support, Center for Clinical Research and Innovation. Kobe City Medical Center General Hospital; miyakoshi@wisdomsprout.com
* Correspondence: kentaroiwata1969@gmail.com; Tel.: (+81-78-382-6296)

Abstract: Ongoing outbreak of pneumonia caused by novel coronavirus (2019-nCoV) began in December 2019 in Wuhan, China, and the number of new patients continues to increase. On the contrary to ongoing outbreak in China, however, there are limited secondary outbreaks caused by exported case outside the country. We here conducted simulations to estimate the impact of potential secondary outbreaks at a community outside China. Simulations using stochastic SEIR model was conducted, assuming one patient was imported to a community. Among 45 possible scenarios we prepared, the worst scenario resulted in total number of persons recovered or removed to be 997 (95% CrI 990-1,000) at day 100 and maximum number of symptomatic infectious patients per day of 335 (95% CrI 232-478). Calculated mean basic reproductive number (R_0) was 6.5 (Interquartile range, IQR 5.6-7.2). However, with good case scenarios with different parameter led to no secondary case. Altering parameters, especially time to hospital visit could change the impact of secondary outbreak. With this multiple scenarios with different parameters, healthcare professionals might be able to prepare for this viral infection better.

Keywords: Novel coronavirus; SEIR model; outside China.

1. Introduction

An outbreak of pneumonia caused by novel coronavirus (2019-nCoV) began in December 2019 in Wuhan, China, and the number of the newly reported cases continues to increase. More than 7,800 cases were reported globally, and 170 of them died as of this writing (January 31, 2020) [1]. Initially, this virus was believed to be transmitted from some wild animals to human, and human to human transmission was limited or nonexistent [2], but it turned out human to human transmission indeed occurs, resulting in thousands of patients in China. As of this writing, 82 confirmed cases were reported outside of mainland China, found in 18 different countries [3]. However, relatively small number of secondary cases after importation of this virus by human to human transmission outside China have been confirmed so far [4-7].

While we do not know the extent of transmissibility of this virus precisely, and do not know how serious these impacts of secondary human to human transmission outside China could be, we developed a mathematical model and simulated the possibility and the risk of secondary outbreak caused by 2019-nCoV outside China, in a developed country with relatively good infectious diseases reporting system and infection prevention practices.

2. Experimental Section

We hypothesized a scenario of one person with 2019-CoV infection entering into a community with population of 1,000. The SEIR model was used, with compartment S, E, I, R stand for susceptible, exposed, infected, and recovered or removed respectively. The model describing the status of each compartment is shown in the following differential equations.

$$\frac{dS(t)}{dt} = -\frac{\beta S(t)I(t)}{N} \tag{1}$$

$$\frac{dE(t)}{dt} = \frac{\beta S(t)I(t)}{N} - \delta E(t) \tag{2}$$

$$\frac{dI(t)}{dt} = \delta E(t) - \nu I(t) \tag{3}$$

$$\frac{dR(t)}{dt} = \nu I(t) \tag{4}$$

Where β is force of infection, or disease transmission rate, δ is inverse of latent period (days), and ν is inverse of infectious period (days), or removal rate. Because of these parameters in developed countries outside China remains unknown as of the current writing, we prepared a combination of parameters to simulate multiple scenarios likely or possible to occur. The followings are the combination of the parameters.

β: (1) 0.01-0.02, (2)0.04-0.06, (3)0.1-0.2, (4)0.4-0.6, (5)0.8-1
δ: (i) 1/4-1/2, (ii) 1/10-1/4, (iii) 1/14-1/10
ν: (a)1/2-1, (b) 1/7-1/2, (c) 1/10-1/7

With 5 scenarios in β, 3 in δ, 3 in ν, we developed 45 scenarios and simulated each. With stochastic imputation, data between upper limit and lower limit of each parameter were assigned randomly.

N is a population size of the community and it is 1,000 in our simulation. Susceptible individuals in class S in contact with the virus entered the exposed class E. Exposed individuals undergo incubation period ranging from 2 to 14 days, before progressing to the infectious class I: Infectious individuals eventually move to R (death or recovered). We assumed no further transmission would occur once a person entered into the status of R. We began the simulation assuming the aggregate of S, E, I, R be 1,000, and simulation started with S=999, E=1, I=0, and R=0.

We constructed mathematical models of prediction for the following 100 days after importation of one infection as follows: We assumed uniform distribution for each parameter. We obtained the number of patients in each status (i.e., S, E, I, and R) at every 0.2 day from the beginning to the 100th day using Markov chain Monte Carlo (MCMC) method. We set a sampling sequence of 200 random samples without warmup. Two-sided 95% credible intervals (CrI) were also calculated.

Basic reproductive number (R_0) was calculated as β/ν by using mean number of 1,000 imputations under the condition of each scenario. Analyses were performed with the use of R software (R Foundation for Statistical Computing).

3. Results

Among 45 scenarios, the worst scenario with the largest number of infected and recovered would occur, was when β was 0.8-1, δ was 1/14-1/10, and ν was 1/10-1/7. The simulation showed total number of the recovered or removed patients of 997 (95% CrI 990-1,000) at day 100 and maximum number of symptomatic infectious patients per day of 335 (95% CrI 232-478) (Figure 1). Calculated mean basic reproductive number (R_0) was 6.5 (Interquartile range, IQR 5.6-7.2).
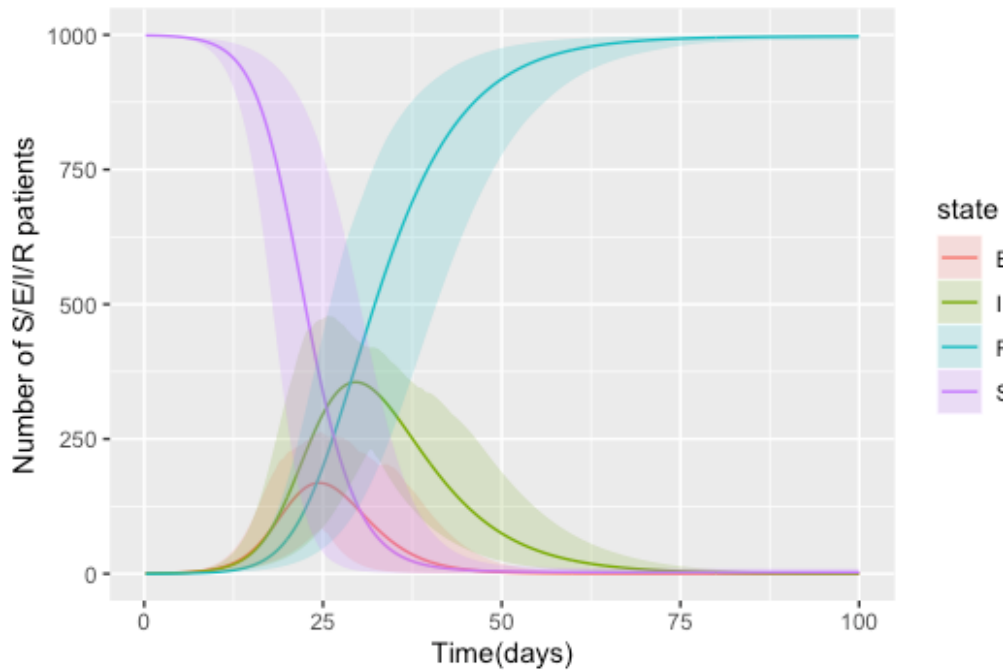
Figure 1. SEIR model with the worst case scenario. Abbreviations S=susceptible E=exposed, I=infected, and R=recovered and removed.

With the best-case scenario where β was 0.01-0.02, δ was 1/4-1/2, and ν was 1/2-1, secondary outbreak did not occur, and total number of the recovered or removed patients were 1 (95% CrI 1-1) at day 100 and maximum number of symptomatic infectious patients per day was 0.2 (95% CrI 0-0.3) (Figure 2). R_0 was 0.021 (IQR 0.016-0.025).
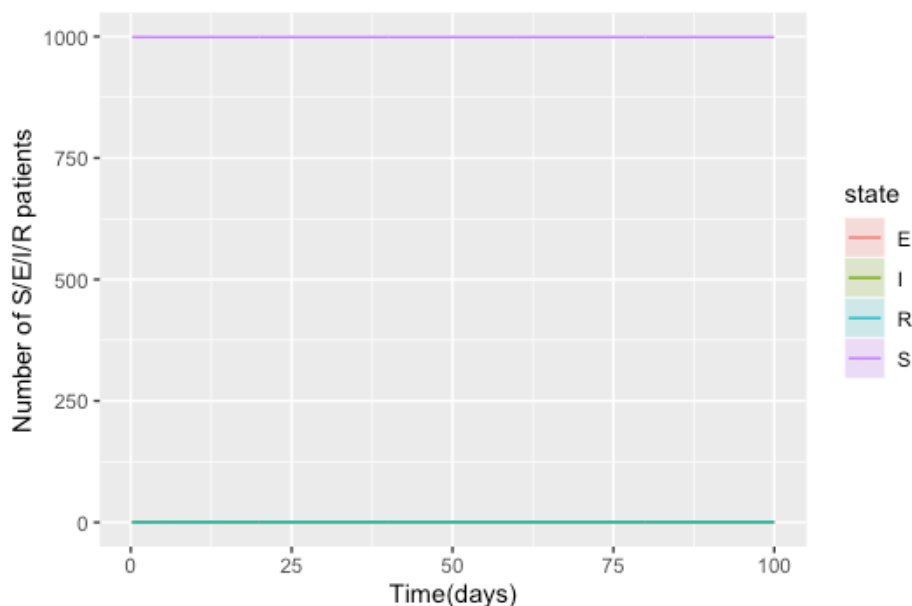

Figure 2. SEIR model with the best-case scenario. Abbreviations S=susceptible E=exposed, I=infected, and R=recovered and removed.

The secondary outbreak did not occur while incrementing each parameters until when the scenario became with β of 0.1-0.2, δ of 1/4-1/2, and ν of 1/10-1/7, when the total number of the recovered or removed patients were 46 (95% CrI 2-252) at day 100 and maximum number of

symptomatic infectious patients per day was 13 (95% CrI 1-79) (Figure 3). R_0 was 1.1 (IQR 0.8-1.4). However, when we increased β to 0.4-0.6, while keeping δ and ν the same, the secondary outbreak did not occur. With the same β of 0.4-0.6, increase the duration until the medical visit to 2 to 7 days, and 7 to 10 days (ν 1/7-1/2, 1/10-1/7 respectively), the total number of the recovered or removed patients increased to 304 (95% CrI 2-919) and 874 (95% CrI 247-994) respectively, with R_0 of 1.4 (IQR 0.9-1.7) and 3.4 (IQH3.4 (IQR 2.5-4.2) respectively. Increasing β to 0.8-1.0 with δ of 1/4-1/2, and ν of 1/2-1 led to total of 187 patients recovered or removed at day 100 (CrI 3-740) with R_0 of 1.1 (IQR 0.9-1.3) (Figure 4). The rest of the simulations and calculated R_0 are shown in the supplementary file.
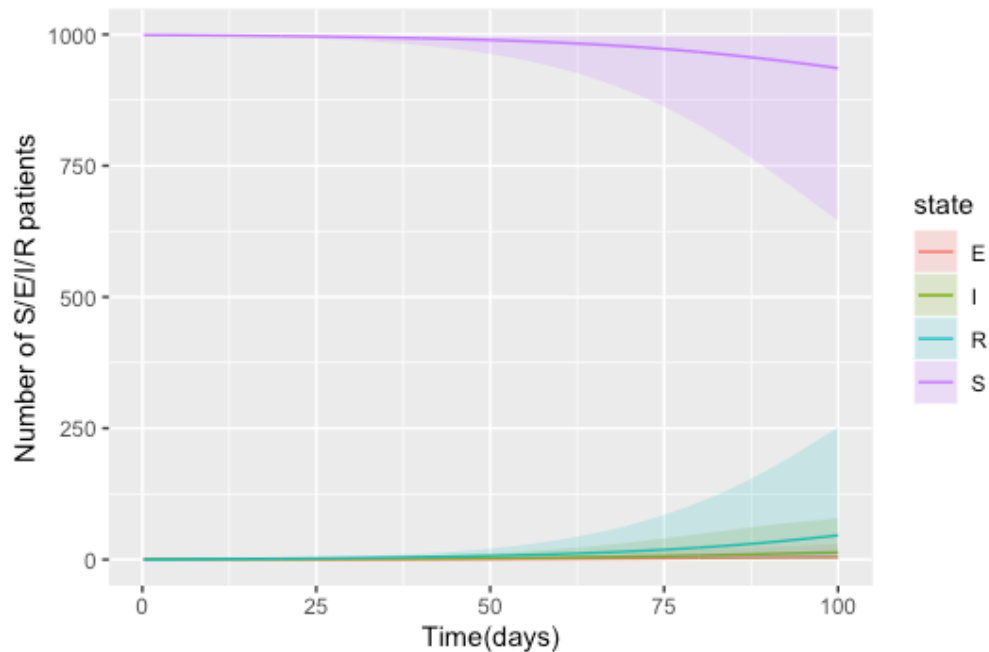
Figure 3. SEIR model with the parameters (β 0.1-0.2, δ 1/4-1/2, and ν 1/10-1/7) when the secondary outbreak started to occur. Abbreviations S=susceptible E=exposed, I=infected, and R=recovered and removed.
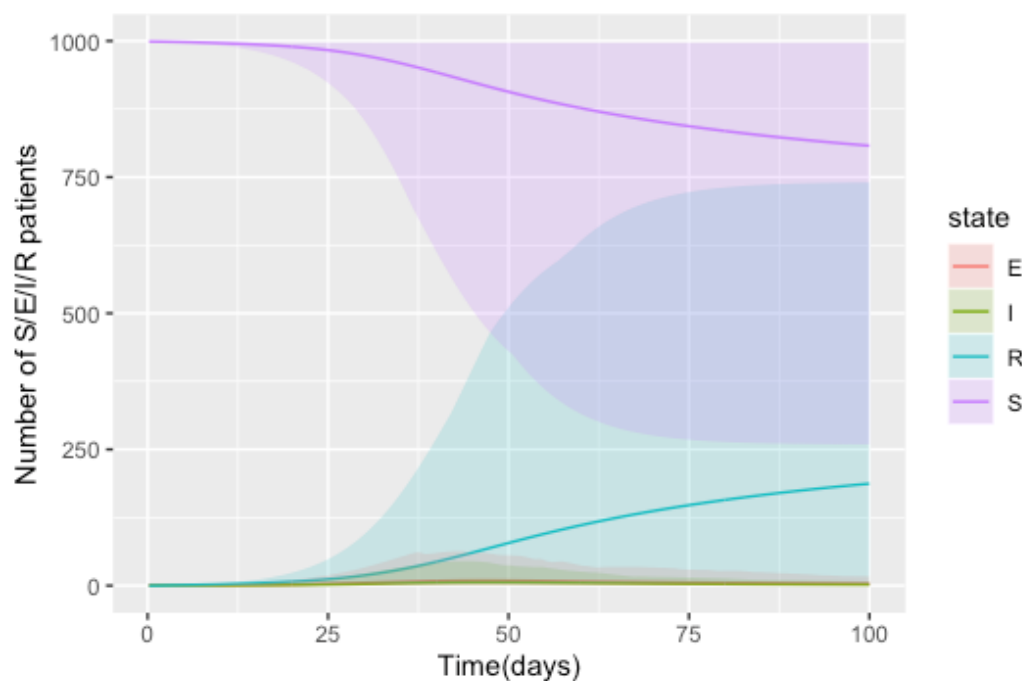
Figure 4. SEIR model with β of 0.8-1.0 but with δ of 1/4-1/2, and ν of 1/2-1. Abbreviations S=susceptible E=exposed, I=infected, and R=recovered and removed.

4. Discussion

The number of new patients diagnosed as 2019-nCoV infection keeps increasing in China as of this writing [3]. Several studies estimated basic reproductive number (R_0) by different methods and they range from 2.2 to 5.5 [10-12]. However, relatively small number of patients had been detected as secondary infected outside China as of this writing [4-7]. Since R_0 is determined not only by virologic nature and biological characteristics of hosts, but also by other factors, such as the number of close contacts with the infected, use of protections such as surgical masks, or timely isolations of patients at health care facilities, published mathematical models based on existing other coronavirus and epidemics within China might not apply to 2019-nCoV infections at a different setting. Our simulation with multiple scenarios indeed demonstrated that shortening the duration from the onset of symptoms to medical visit could decrease the number of infected even with the same level of force of infection. With advanced reporting system and adequate infection control practices in health care facilities, transmissibility of this virus could be decreased in other developed countries from one in Wuhan. Therefore, the estimation of the risk of secondary outbreaks separately, like what we have done, has values in infection control in other nations.

Our results suggest that with hundreds of newly diagnosed 2019-nCoV infections could occur with a bad scenario when a person with the infection entered into a community of a thousand. This means we need to be alerted of the possibility that secondary transmission and spread of this virus as a very realistic possibility, and be prepared for this future possibility. On the other hand, we also demonstrated that with a good scenario, a secondary outbreak outside might not occur, as seen in most countries, which found 2019-nCoV imported cases as of this writing. Also, with improving alert system with early recognition of the infected persons could decrease or hold a secondary outbreak.

Our study does have several inherent limitations. First, because most parameters regarding 2019-nCoV remains unknown, especially ones at different countries other than China, we had to rely on arbitrary numbers, and they may not be accurate. Second, there is hypothesis that asymptomatic patients could be infectious to others [13], although how frequently this occurs remains unknown. We did not incorporate this hypothesis into our analysis. Third, we assumed that there would be no nosocomial outbreak of 2019-nCoV in a region we hypothesized, presuming adequate infection control practices could prevent this to occur. However, breach of infection control practice could happen in any area and we had nosocomial outbreaks of imported infections in developed nations such as Canada [14], the United States [15], and South Korea [16]. Forth , we hypothesized that 2019-nCoV infection would lead to fairly long-lasting immunity and did not assume the possibility of re-infection to the infected persons. With these limitations, we need to gain more data, and to study the risk of this new infection and the virus further.

5. Conclusions

Hundreds of secondary infections by 2019-nCoV is possible in a developed country when a person with the infection was introduced into a community. Adequate reporting system and infection control practice, however, could mitigate the risk to certain level according to our simulations.

References

1. Coronavirus Live Updates: W.H.O. Declares a Global Health Emergency. The New York Times [Internet]. 2020 Jan 30 [cited 2020 Jan 31]; Available from: https://www.nytimes.com/2020/01/30/world/asia/coronavirus-china.html

2. Perlman S. Another Decade, Another Coronavirus. New England Journal of Medicine. 2020 Jan [cited 2020 Jan 28] Available from: https://www.nejm.org/doi/full/10.1056/NEJMe2001126?query=recirc_curatedRelated_article

3. World Health Organization. Novel Coronavirus (2019-nCoV)Situational Report 10 . January 30, 2020. [cited 2020 Jan 31]; Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

4. Phan LT, Nguyen TV, Luong QC, Nguyen TV, Nguyen HT, Le HQ, et al. Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. New England Journal of Medicine. 2020 [cited 2020 Jan 31]; Available from: https://www.nejm.org/doi/full/10.1056/NEJMc2001272

5. Germany confirms first human coronavirus transmission in Europe. The Guardian [Internet]. 2020 Jan 28 [cited 2020 Jan 31]; Available at: https://www.theguardian.com/science/2020/jan/28/germany-confirms-first-human-coronavirus-transmission-in-europe

6. Japan reports first domestic transmission of coronavirus | The Japan Times [Internet]. [cited 2020 Jan 31]. Available from: https://www.japantimes.co.jp/news/2020/01/28/national/japan-first-domestic-transmission-coronavirus/#.XjNvBhfgqKU

7. Coronavirus: US reports first person-to-person transmission - BBC News [Internet]. [cited 2020 Jan 31]. Available from: https://www.bbc.com/news/world-us-canada-51316915

8. Symptoms of Novel Coronavirus (2019-nCoV) | CDC [Internet]. 2020 [cited 2020 Jan 31]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/about/symptoms.html

9. Ridenhour B, Kowalik JM, Shay DK. Unraveling R0: Considerations for Public Health Applications. Am J Public Health. 2014;104:e32–41.

10. R Liu T, Hu J, Kang M, Lin L, Zhong H, Xiao J, et al. Transmission dynamics of 2019 novel coronavirus (2019-nCoV). bioRxiv. 2020;2020.01.25.919787.

11. Zhao S, Ran J, Musa SS, Yang G, Lou Y, Gao D, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. bioRxiv. 2020;2020.01.23.916395.

12. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia | NEJM [Internet]. [cited 2020 Jan 31]. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2001316?query=featured_home

13. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. NEMJ. 2020 Jan 30; [Internet]. [cited 2020 Jan 31]. Available https://www.nejm.org/doi/full/10.1056/NEJMc2001468?fbclid=IwAR2GDaT0Wb3BcRDic-0YIAmJ0Y5yE96xXxkiAYzYMUfwqIYDIsEraiKkRIM

14. Varia M, Wilson S, Sarwal S, McGeer A, Gournis E, Galanis E, et al. Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. CMAJ. 2003;169:285–92.

15. Parra JM, Salmerón OJ, Velasco M. The First Case of Ebola Virus Disease Acquired outside Africa. New England Journal of Medicine. 2014 Dec 18;371:2439–40.

16. Ki M. 2015 MERS outbreak in Korea: hospital-to-hospital transmission. Epidemiol Health [Internet]. 2015 Jul 21 [cited 2020 Jan 28];37. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4533026/