Susceptible, Exposed, Infected and Removed (SEIR) model for Coronavirus spread. The Pullman introduction case

Most models I have seen to this date focusing on SARS-CoV-2 are of the SEIR type. Something to be recognized is that there is a lot of variability in the estimates of R_0 ranging from 2 to 3.5 Most of the estimates seem to converge towards $R_0 = 2.3$. So I am going to assume that this is a reasonable estimate. A modified SEIR model from influenza has been used to estimate the number of cases progression in Wuhan[1] and I further modified it to include mortality:

$$\dot{S} = -\beta SI/N \tag{1}$$
$$\dot{E} = \beta SI/N - \sigma E \tag{2}$$
$$\dot{I} = \sigma E - (\gamma + \mu)I \tag{3}$$
$$\dot{R} = \gamma I \tag{4}$$
$$N = S + E + I + R \tag{5}$$

where β is the transmission rate, σ is the infection rate (development of infection) and it is usually estimated as the inverse of the incubation period, γ is the recovery rate estimated as the inverse of the infectious period, and μ is the mortalty rate associated to the infection.

For this we need to make reasonable assumptions about incubation period and the infectious period. It has been assumed that $\sigma = 1/5.2$ under the estimation that the incubation period is 5.2 days[2]. In Wuhan, it was estimated that hospitalization period of recovered patients was 12.39 ± 4.77 days[3,4]. For simplicity we assume the average of the infectious period to be then 12.39 and $\gamma = 1/12.39 = 0.0807$. I had originally considered the ceiling of the recovery time, but given the general health status of our population, it seems reasonable to make the estimations with the average.

R_0 is usually estimated as the leading eigenvalue from the FV^{-1} matrix that describes the terms for the acquisition of the infections and the transition between states. In the simplest SEIR model that does not consider the age structure we can then simply describe it as:

$R_0 = \frac{\beta\sigma}{\sigma\gamma}$

The transmission rate then can be estimated from the relationship $\beta = R_0\gamma$ from this model. Given that the mean R_0 has been estimated to be 2.3 across multiple studies[1,2,5,6], we can make a conservative estimate of β assuming that recovery takes the ceiling of the distribution (17.16 days), that gives us $\beta = 2.3/17.16 = 0.147$.

At this point the mortality rate by SARS-CoV-2 seems to be remarkably different between individuals of different ages[7]. In this study, following 72,314 cases in Wuhan 44,672 (62%) were classified as confirmed cases of COVID-19, the number of suspected cases was 16186 (22%), the number of diagnosed cases 10,567 (15%) and the number of asymptomatic 889 (1%). I am going to assume the distribution of fatality rate from:c

1. 2.3% (1023 of 44672 confirmed cases)
2. 14.8% in patients aged ⩾80 years (208 of 1408)
3. 8.0% in patients aged 70-79 years (312 of 3918)
4. 49.0% in critical cases (1023 of 2087)

From these, I am going to assume the mortality rate (μ_o) of individuals > 70 year old to be 8% or 11.4% in a 2 months period to model the spread of disease in an age structured population for individuals, and consider the mortality rate (μ_b) for the rest of the population to be 2.3% in a 2 months period in which these observations were done (60 days). The mortality rate for >70 yo would then be $\mu_o = 0.0013$ *deaths/day* or $\mu_o = 0.0019$ *deaths/day* and the mortality rate of rest of the population is $\mu_b = 0.0004$.

All scenarios were examined using simulations in R 3.6.4 using the *deSolve* package to explore numerically the dynamics.

To set the starting point for the simulations we assume a naive susceptible population of size 1M. We perform simulations under two different introduction scenarios, all assuming that exposed individuals arrive to town. The two scenarios assume: i) that 1 exposed individual ($E_b = 1$) introduces the disease to town; and ii) that 10 exposed individuals ($E_b = 10$) introduce the disease to town.

Modified Wang model (no population structure yet)

Scenario 1: introduction of 1 exposed (E) individual

Under the assumption that 1 exposed individual arrives to a city of 1M people, we examine the expected dynamics after 120 days and 365 days after introduction. Figure 1 shows that after 120 days after the introduction of a single infected individual we would expect that approximately 2101

individuals would have been infected (0.21% of the population). Out of these, we would expect to see at 120 days of infection: 502 exposed individuals (0.05% of the population), 683 infected individuas (0.07% of the population) and 913 recovered individuals (0.091% of the population).

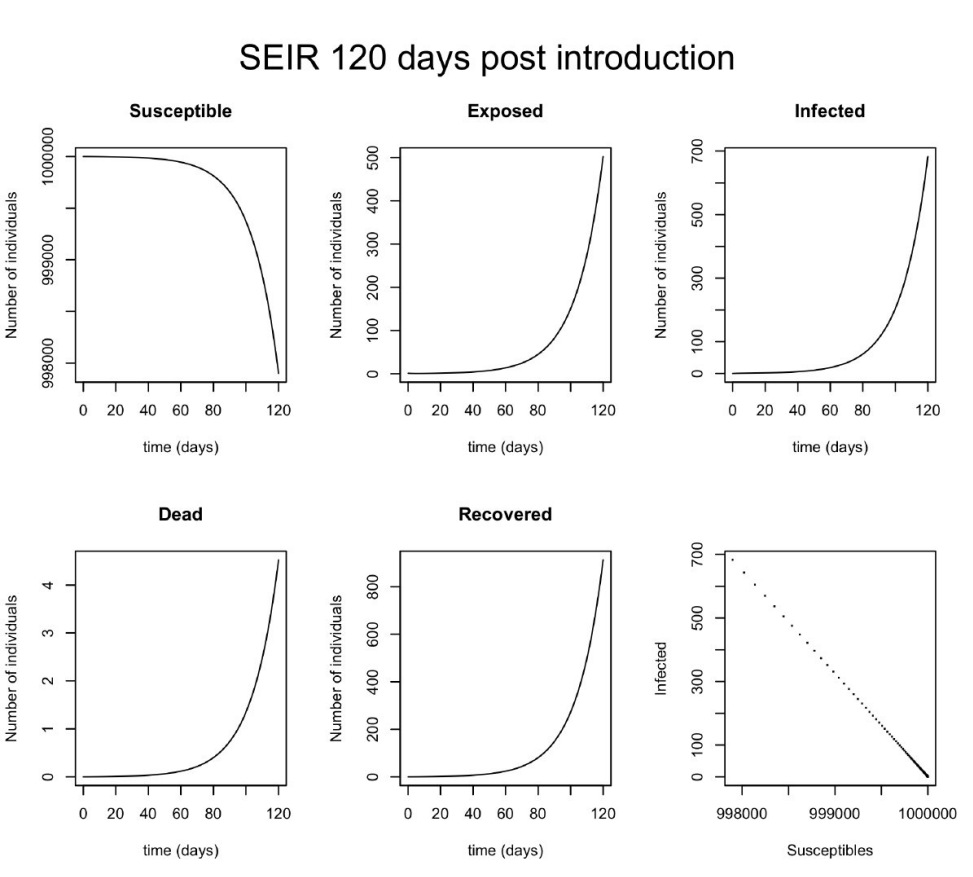

Figure 1. Dynamics of Susceptible, Exposed, Infected, and Recovered individuals during the intial phase of the outbreak caused by 1 exposed individual.

Without mitigation, if we allow the simulations to continue for 365 days (1 year) we predict that at the peak of the epidemic we will have 140,710 infected individuals at 234 days after the introduction of a single exposed individual. In this scenario, after 12 months of transmission 860,716 individuals (86%) of the population could have been infected (Figure 2).

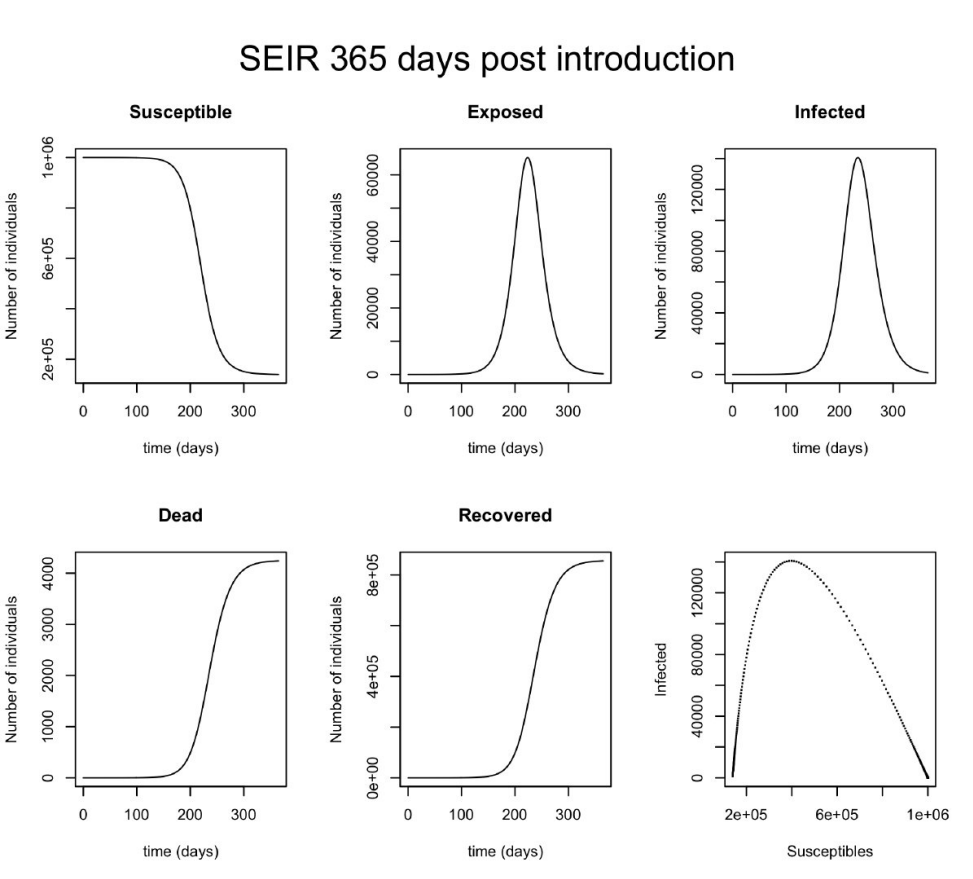

Figure 2. Dynamics of Susceptible, Exposed, Infected, and Recovered individuals for 12 months after introduction after 1 exposed individual.

I have not included here other scenarios with multiple individuals exposed being introduced to the population but we have examined those as well (for $E = 10$ and $E = 100$). The natural consequences of the introduction of more exposed/infected individuals is the acceleration of the epidemic. If interested in these just shoot me a message and I am happy to provide them.

What about mitigation? We examine what the consequence of reducing the transmission rate to 2/3 of its current value

Under the assumption that 1 exposed individual arrives to a city of 1M people, we examine the expected dynamics after 120 days and 365 days after introduction if mitigation is implemented 30 days post introduction. Figure 3 shows that after 120 days after the introduction of a single infected individual (90 days after intervention) we would expect that approximately 134 individuals would have been infected (0.013% of the population), a significant reduction from the 2101 individuals expected to have been infected without mitigation . Out of these, we would expect to see at 120 days of infection: 17 exposed individuals (0.002% of the population), 31 infected individuas (0.003% of the population) and 86 recovered individuals (0.009% of the population).

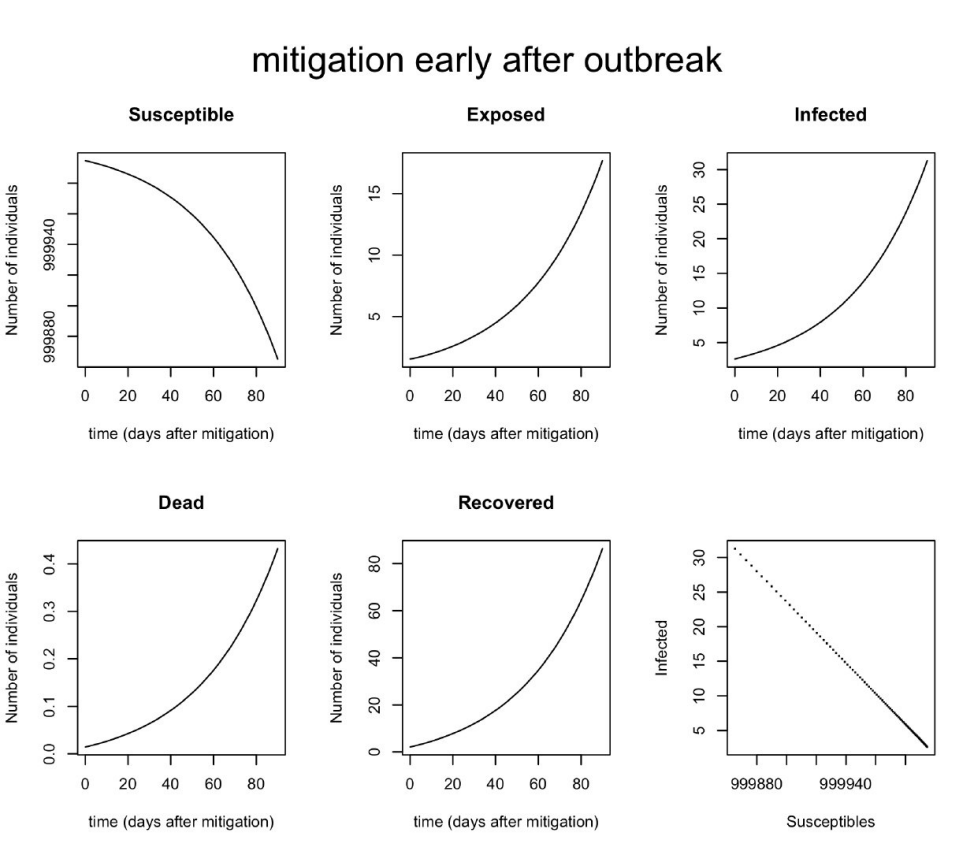

Figure 3. Dynamics of Susceptible, Exposed, Infected, and Recovered individuals during the intial phase of the outbreak caused by 1 exposed individual and mititgation is implemented 30 days post introduction (transmission rate = 2/3 of original value)

With mitigation, the epidemic spreads longer in time. The specific time here is not of relevance here because it strongly depends on other measures aimed at mitigating the epidemic. Remember, we have only considered here the reduction in transmission. If we allow the simulations to continue for 630 days we predict that at the peak of the epidemic we will have 47,888 infected individuals at 411 days after the introduction of a single exposed individual. In this scenario, after 12 months of transmission 599,418 individuals (60%) of the population could have been infected (Figure 4).

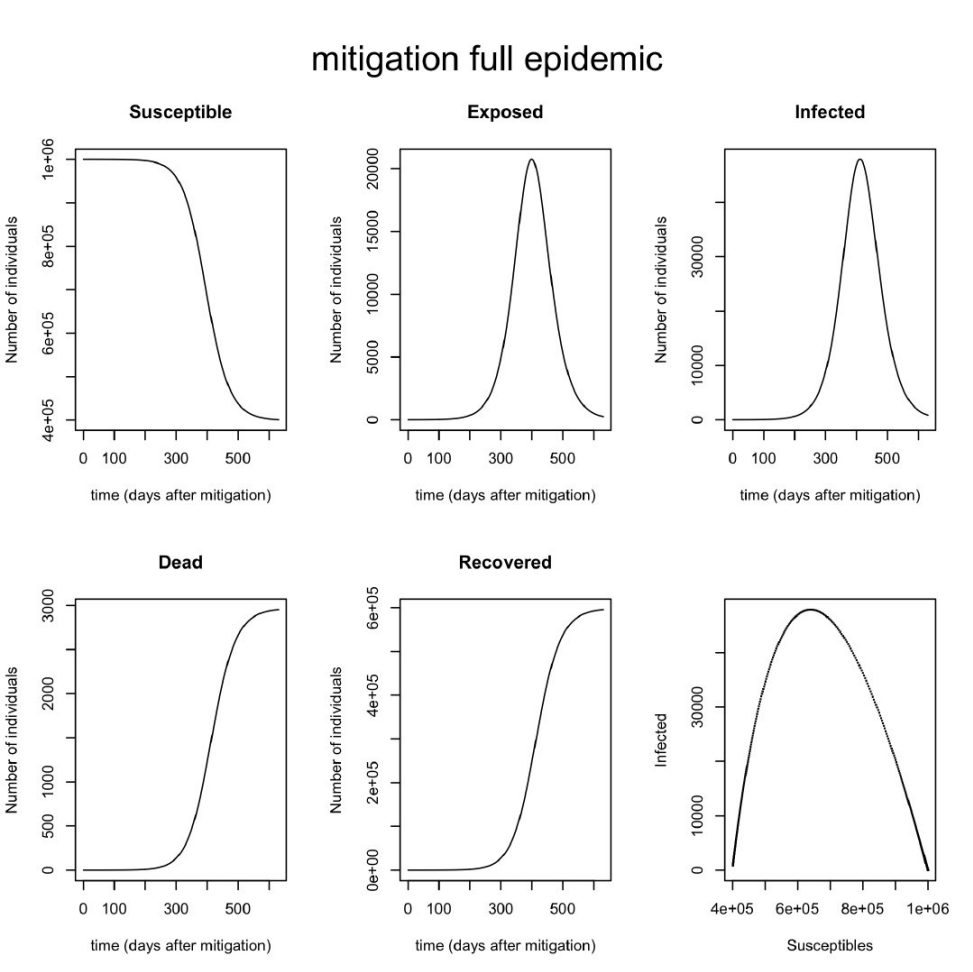

Figure 4. Dynamics of Susceptible, Exposed, Infected, and Recovered individuals during the intial phase of the outbreak caused by 1 exposed individual and mititgation is implemented 30 days post introduction (transmission rate = 2/3 of original value)

To more easily see the impact of mitigation take a look at Figure 5. It shows how not only the curve is flattened but you can start to see that the total number of cases is also reduced. More on this will come in a later delivery.

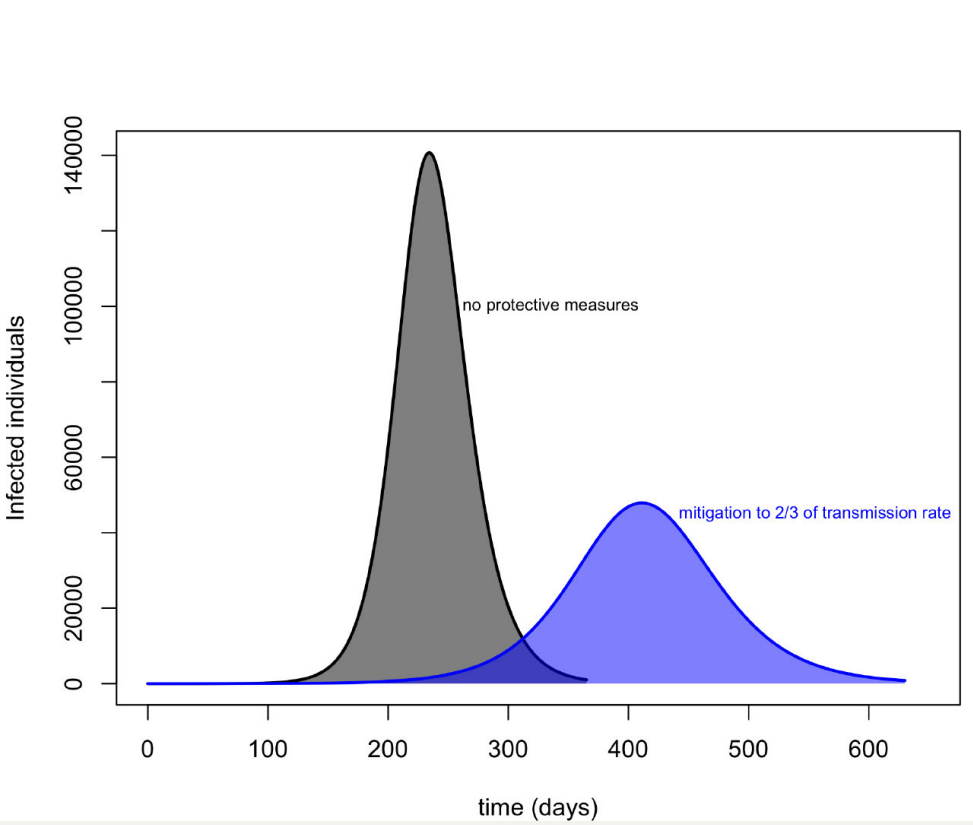

Figure 5. Comparison of the dynamic of infected individuals with and without mitigation.

We are also interested in examining what the impact of mitigation being implemented at different times and relaxing it at different times has on the dynamics. This is something that Mark Tanaka has alreday started looking at.

Structured SEIR model for the spread of SARS-CoV-2

Up to this point I have not started examining simulations of more elaborate models, I am going to introduce the age structured model I have been started to develop. The motivation for this is my interest in assessing what is going to be the relative impact of the non-risk population to the outcome of the epidemic for those at risk.

This is just a reminder of information already presented. At this point the mortality rate by SARS-CoV-2 seems to be remarkably different between individuals of different ages[7]. In this study, following 72,314 cases in Wuhan 44,672 (62%) were classified as confirmed cases of COVID-19, the number of suspected cases was 16186 (22%), the number of diagnosed cases 10,567 (15%) and the number of asymptomatic 889 (1%). I am going to assume the distribution of fatality rate from[7]:

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4. 49.0% in critical cases (1023 of 2087)

From these, We are going to separate the population in two strata: low risk (l) and high risk (h) and have a separate mortality rate (μ_h) for individuals > 70 year old to be 8% or 11.4% in a 2 months period to model the spread of disease in an age structured population for individuals, and consider the mortality rate (μ_l) for the rest of the population to be 2.3% in a 2 months period. The mortality rate for >70 yo would then be $\mu_h = 0.0013$ or $\mu_h = 0.019$ and the mortality rate of rest of the population is $\mu_l = 0.0004$. To simplify matters, we will assume that for a period of three months (120 days) the mortality in the population younger than 70 can be neglected.

We then modified the previous model with equations 6-9 to include mortality and two different categories of individuals (higher risk with sub-index *h* and low risk with sub-index *l*):

$$\dot{S_h} = -\beta S_h (I_h + I_l)/N \tag{6}$$
$$\dot{S_l} = -\beta S_l (I_h + I_l)/N \tag{7}$$
$$\dot{E_h} = \beta S_h (I_h + I_h)/N - \sigma E_h \tag{8}$$
$$\dot{E_l} = \beta S_l (I_h + I_l)/N - \sigma E_l \tag{9}$$
$$\dot{I_h} = \sigma E_h - (\gamma + \mu_h) I_h \tag{10}$$
$$\dot{I_l} = \sigma E_l - (\gamma + \mu_l) I_l \tag{11}$$
$$\dot{R_h} = \gamma I_h \tag{12}$$
$$\dot{R_l} = \gamma I_l \tag{13}$$
$$\dot{deaths_h} = \mu_h I_h \tag{14}$$
$$\dot{deaths_l} = \mu_l I_l \tag{15}$$

After conversations with Ben Kerr, we have a modified version of this model to explicitely examine the reduction in *contact rates* among the high risk and low risk classes of individuals. On this model we allow for the contact rates (θ) of high risk and low risk individuals in the infected and susceptible categories to be different.

$$\dot{S}_h = -\beta S_h \theta_{sh} (I_h \theta_{ih} + I_l \theta_{il})/N \quad (16)$$
$$\dot{S}_l = -\beta S_l \theta_{sl} (I_h \theta_{ih} + I_l \theta_{il})/N \quad (17)$$
$$\dot{E}_h = \beta S_h \theta_{sh} (I_h \theta_{ih} + I_h \theta_{il})/N - \sigma E_h \quad (18)$$
$$\dot{E}_l = \beta S_l \theta_{sl} (I_h \theta_{ih} + I_l \theta_{il})/N - \sigma E_l \quad (19)$$
$$\dot{I}_h = \sigma E_h - (\gamma + \mu_h) I_h \quad (20)$$
$$\dot{I}_l = \sigma E_l - (\gamma + \mu_l) I_l \quad (21)$$
$$\dot{R}_h = \gamma I_h \quad (22)$$
$$\dot{R}_l = \gamma I_l \quad (23)$$
$$\dot{deaths}_h = \mu_h I_h \quad (24)$$
$$\dot{deaths}_l = \mu_l I_l \quad (25)$$

The code for the figures shared in twitter can be accessed at: https://github.com/evokerr/SEIR_Risk_Model/

The code for the previos simulations is available in the repository.

References

[1] Wang H, Wang Z, Dong Y, et al. Phase-adjusted estimation of the number of Coronavirus Disease 2019 cases in Wuhan, China. *Cell Discov*. 2020;6:10. Published 2020 Feb 24. doi:10.1038/s41421-020-0148-0

[2] Li, Q. et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2001316 (2020).

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[4] Yang, Y. et al. Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China. *medRxiv*. https://doi.org/10.1101/2020.02.10.20021675 (2020).

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