Mathematical Modeling on Tomato Flu Outbreak in Kerala, India

Introduction

Tomato flu[1], a self-limited disease, is caused by enterovirus(EV) Coxsackievirus A16(CA16). As it is confirmed as the variant of Hand, Foot, and Mouth Disease(HFMD), it has the same mode of transmission spreading through faces and fluid in the spots. Moreover, clinicians in Kerala had confirmed that it is not transmitted by mosquitoes.Differently from HFMD, Tomato Flu shows sign of symptoms as presence of tomato-like red welts all over the body. The control measure for this disease follows the same procedure as in HFMD which isolated the patient for 2 weeks since the disease will resolve without treatment within 1-2 weeks after infections and there is no record of a single death from this disease.

This project aims to propose the intervention and also assess the efficacy of high contact between infected population and susceptible population as the main major factor driving the Tomato flu endemic in Kerala, India.

Parameter

The relative parameter used in the mathematical model is gathered from several sources such as medical journals, news, articles described as followed:

Variable Name	Description	Value	Source of Information
R0	Reproductive Number	1 - 7	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5503211/, https://www.nature.com/articles/srep27500
gamma(γ)	Duration of infectiousness	7-10 day $^{-1}$	https://www.bmj.com/content/378/bmj.o2101.long
sigma(σ)	Duration of Incubation	~4.5 day $^{-1}$	https://www.mayoclinic.org/diseases-conditions/hand-foot-and-mouth-disease/symptoms-causes/syc-20353035
P	children population in Kerala	3,400,000	https://www.populationpyramid.net/india/2022/
Beta(β)	Transmission rate	Gamma * R0	estimation

Compartment Model

Used as a baseline model structure for infectious disease, the SIR model has proven itself as a basis of mathematical model used for observing the trend of disease which is likely to occur in the near future and predicting the direction of the trend when some of the parameters are altered. Likewise, since Tomato Flu is an infectious disease, The SIR model should perform as good as it should be. However, as the information of the incubation period is available, the Exposure population is introduced resulting in The SEIR model. Four ordinary differential equations including S, the susceptible population, E, the exposed population, I, the Infected population, and R, the recovered population:

$$\begin{cases} S = -S\lambda, \\ E = S\lambda - \sigma E, \\ I = \sigma E - \gamma I, \\ R = \gamma I, \end{cases}$$

Where lambda(λ) = $\beta * \frac{I}{P}$

Case Report Data

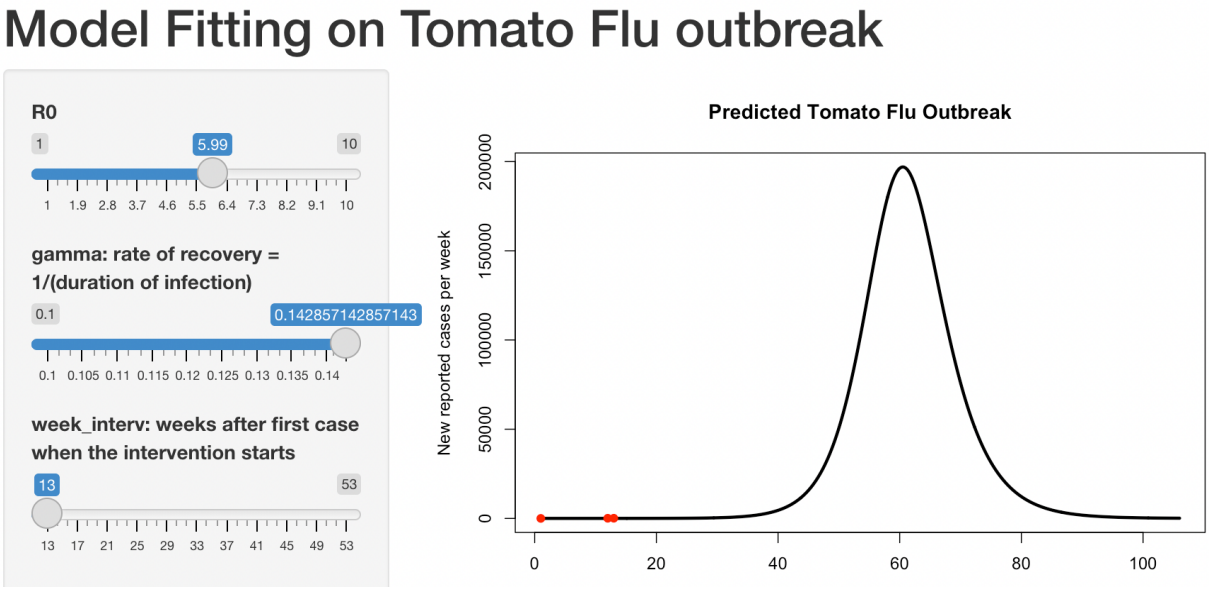
Due to the novelties of the disease and the resemblance of symptoms to the main variant which could lead to the misdiagnosis, case report information publicly available on the internet is limited. So far, the past case report since the first case emerge is described as followed:

Date	Number of Cases	Weeks after First case	Source
6 May 2022	1	0	https://www.forbes.com/sites/brucelee/2022/08/26/new-tomato-flu-outbreak-has-left-over-100-children-ill-in-india/?sh=783570fd222a
26 July 2022	82	12	https://www.forbes.com/sites/brucelee/2022/08/26/new-tomato-flu-outbreak-has-left-over-100-children-ill-in-india/?sh=783570fd222a

~ August 2022	100	13	https://www.forbes.com/sites/brucelee/2022/08/26/new-tomato-flu-outbreak-has-left-over-100-children-ill-in-india/?sh=783570fd222a

Model Fitting

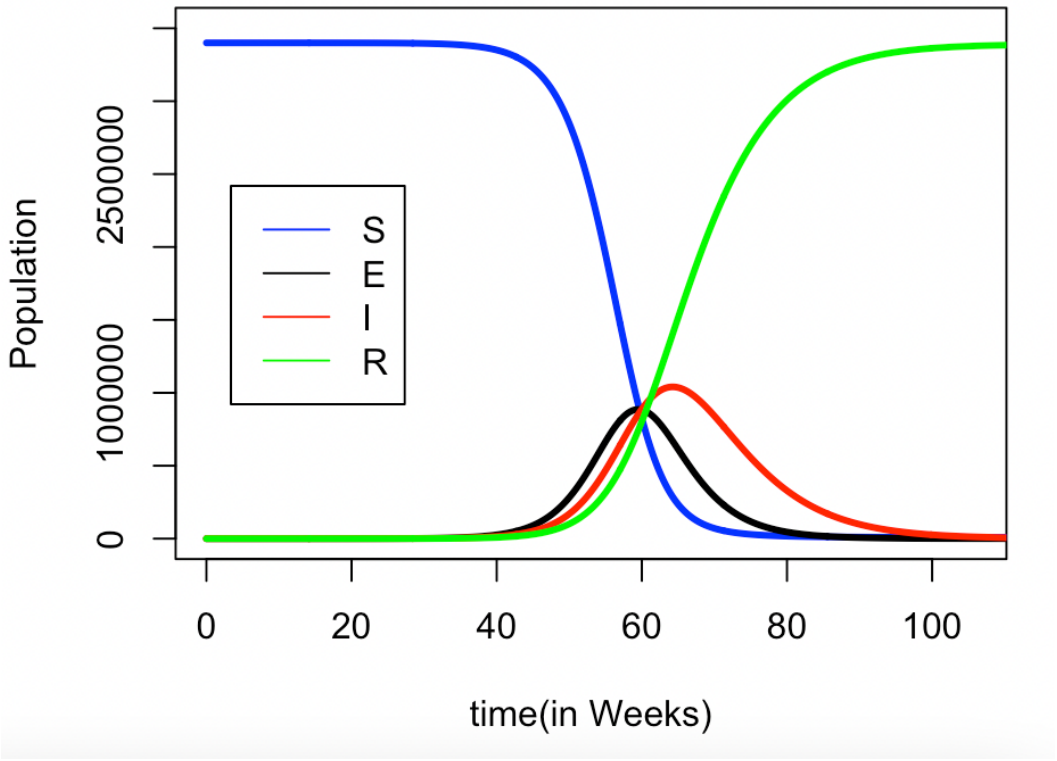
Due to the uncertainty of some parameter resulting in a ranging value, the model fitting approach is then adopted to find the best fitting value of each parameter. For this case, the root mean squared deviation as an optimization function is used to evaluate the fitness of the model.



After fitting data of case report to the model, the algorithm suggest that best value for R0 and gamma(γ) should be 5.99 and 1/7 respectively.

Disease modeling

After estimating the best fitted value of parameters, All of the information is then used to construct the disease model.



From the result, the model indicates that the number of latents will increase around week 40 after the first case appears. Later on, Number of Infected will be noticeable in the population around week 50. During week 60 to 70 is the time where the infected population including the exposed and infected group became the majority of the population and reached its peak. However, after week 70, the number of infected begins to decline or herd immunity stage. On the other hand, the recovered population gradually accumulates in the first state and dramatically rises along with the infected population during week 50. Eventually, after week 100 or around 2 years is where the state which is endemic is ended and more than 90 percent of the population has immunity against this disease.

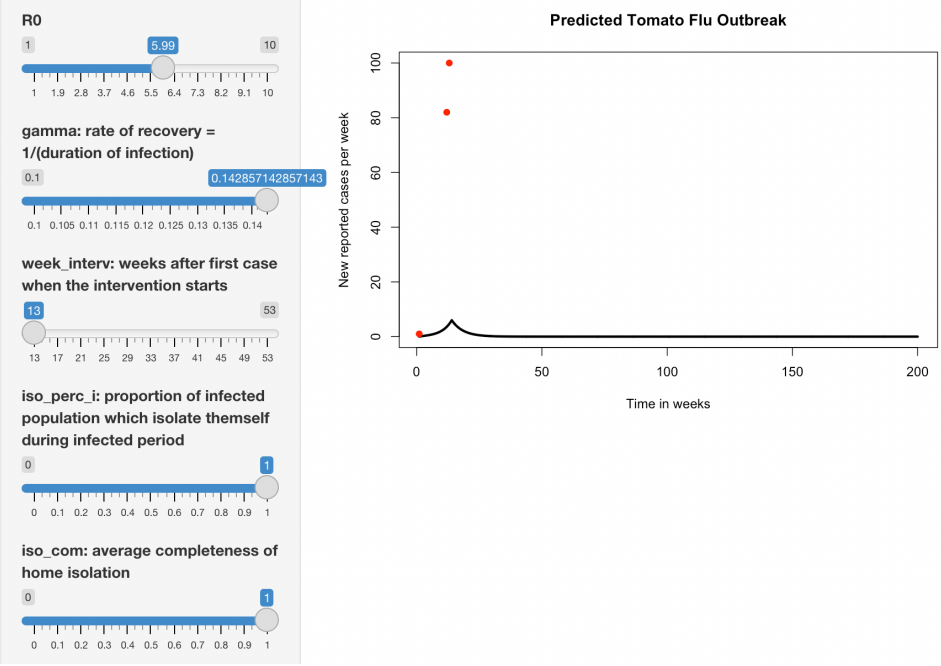
Apply Intervention

As disease is self-limited, nonfatal, and currently could not be prevented by vaccination, acts of isolation after being infected should be the most effective way to obstruct the pandemic. In an ideal case, the isolation would be able to reduce the number of infections as it reduces the contact between infected population and susceptible population. The recommended isolation would be around 1-2 week to reduce the risk of spreading the disease. Accordingly, two factors related to the isolation included in the model which directly altered the rate of infection(λ) which are iso_perc, the percentage of infected population which perform the isolation, and iso_com, the average percentage of completeness of isolation. However, attention should be drawn to both factors as it greatly impacts the direction of the outbreak. The relation of two factor and rate of infection(λ) is describe as:

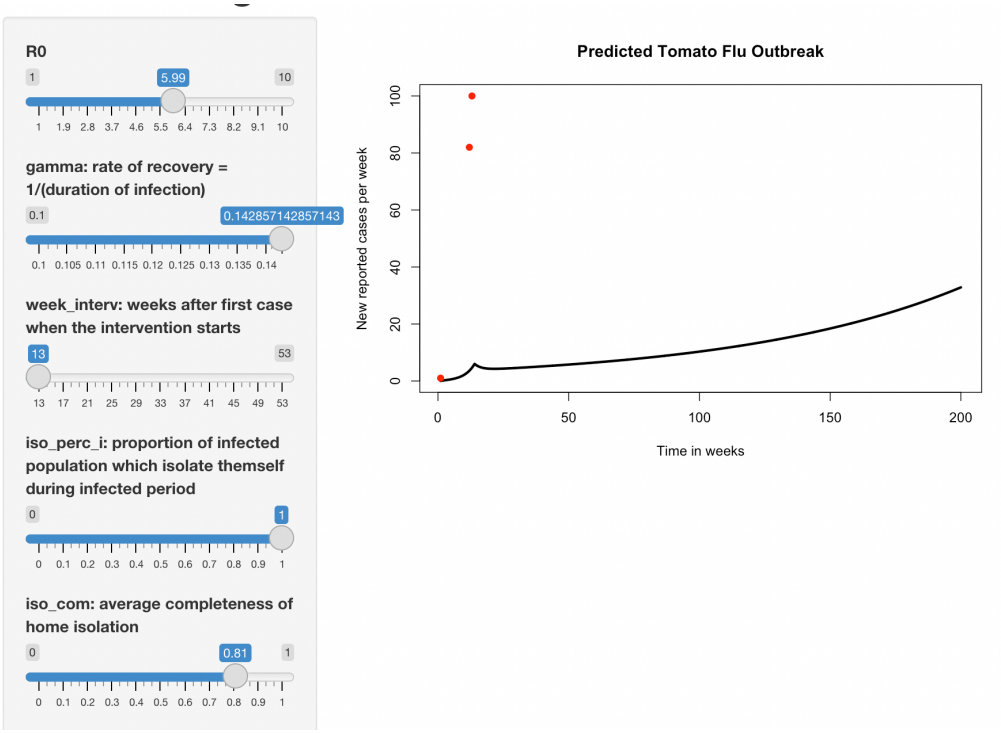
$$\lambda = Isolate * \beta * I / P$$

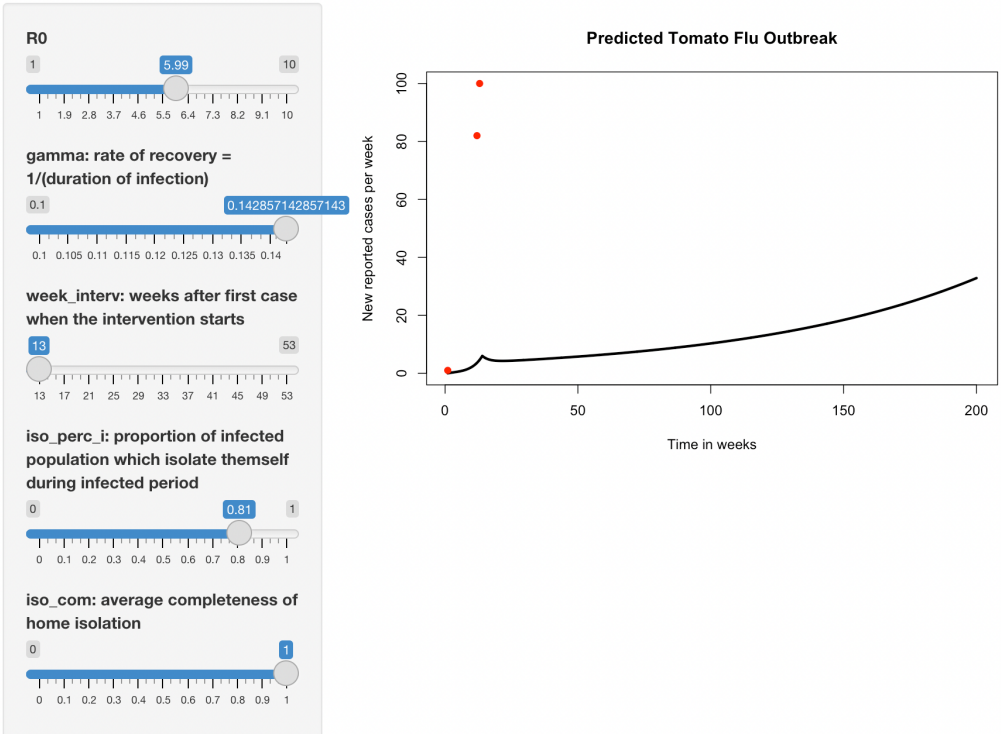
$$where\ Isolate = Iso_com * Iso_perc$$

The intervention is then applied to the model.

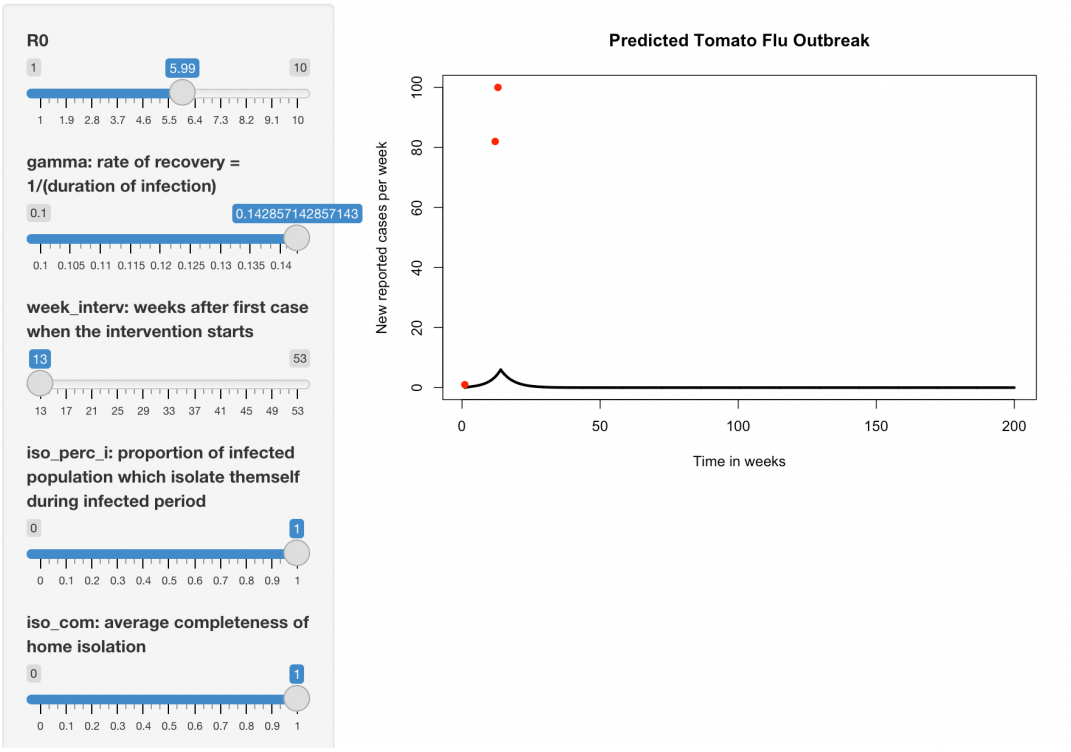


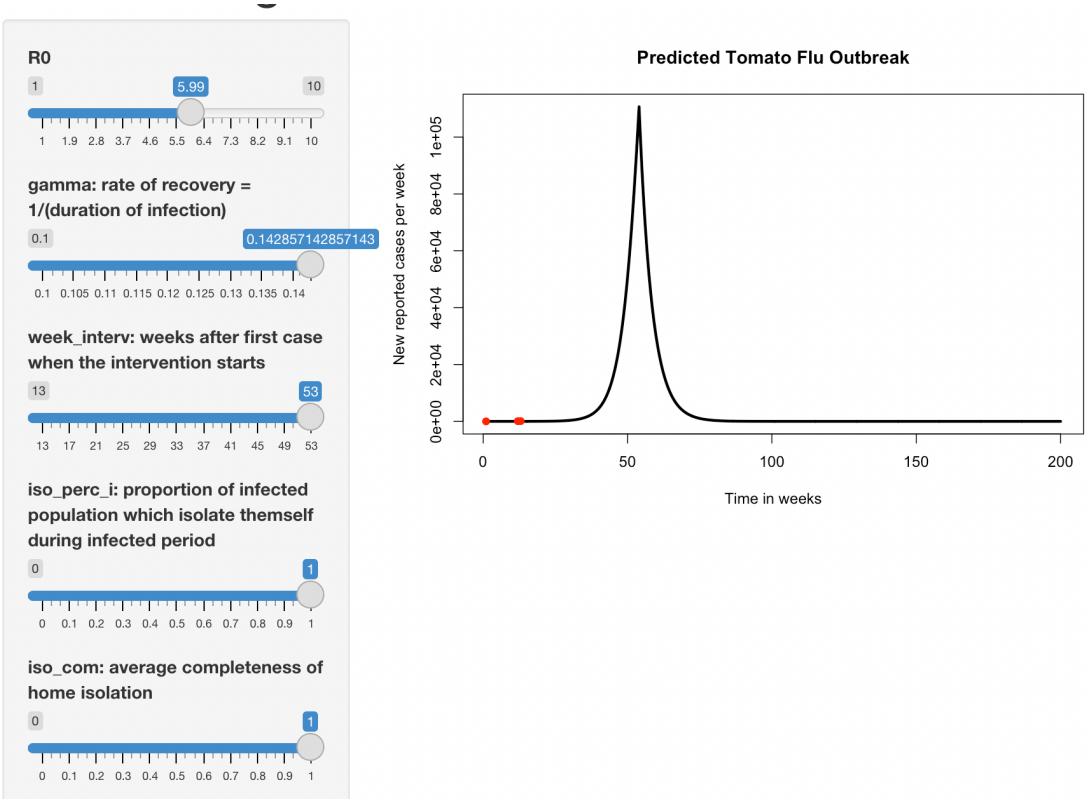
The figure above shows the ideal case where intervention is strictly performed, all of the infected cases strictly followed the intervention act resulting in the non occurrence of the endemic and the disease will disappear before week 50.





As the proportion of the infected population acts of isolation or completeness of isolation is lowered to 80 percent, It could result in a longer period of endemic disease. This would take longer for disease to disappear and lead to the higher chance of spreading the disease to nearby states resulting in a pandemic.


R0
1
5.99
10
1 1.9 2.8 3.7 4.6 5.5 6.4 7.3 8.2 9.1 10
gamma: rate of recovery = 1/(duration of infection)
0.1
0.142857142857143
0.1 0.105 0.11 0.115 0.12 0.125 0.13 0.135 0.14
week_interv: weeks after first case when the intervention starts
13
53
13 17 21 25 29 33 37 41 45 49 53
iso_perc_i: proportion of infected population which isolate themself during infected period
0
1
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
iso_com: average completeness of home isolation
0
1
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Predicted Tomato Flu Outbreak
New reported cases per week
0 20 40 60 80 100
0 50 100 150 200
Time in weeks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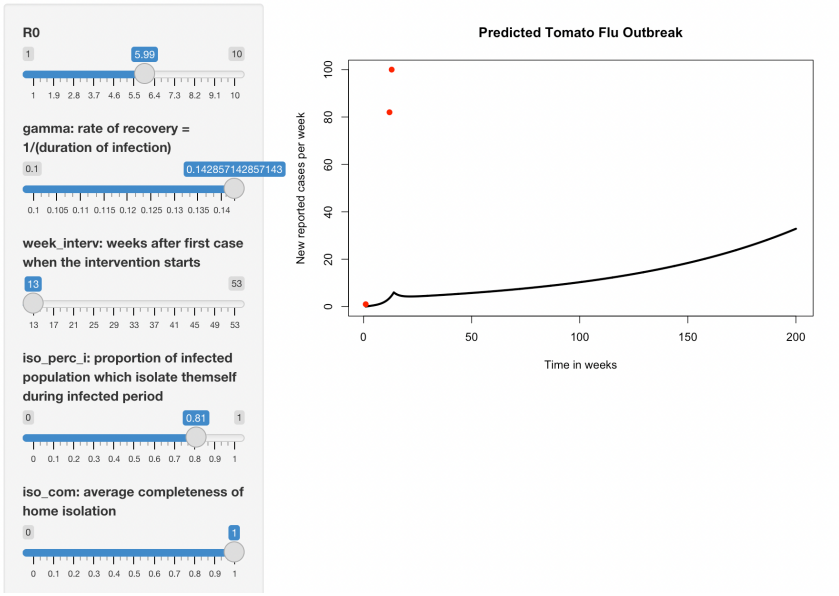
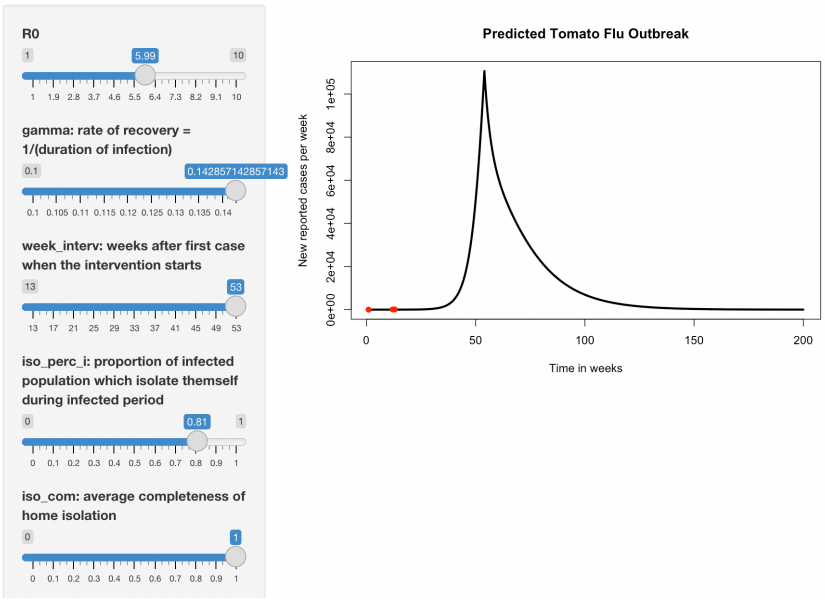
Predicted Tomato Flu Outbreak
New reported cases per week
0e+00 2e+04 4e+04 6e+04 8e+04 1e+05
0 50 100 150 200
Time in weeks

Sooner intervention applications resulting in a better situation to end the endemic are only true when most of the population followed the act of the intervention.





For the case where 81 percent of the infected population followed the intervention or completed the isolation, It would turn out that sooner intervention application will longer the period of endemic while later intervention will increase the number of infected population.

Conclusion

In summary, the Tomato flu outbreak in Kerala, India turned out to be one of the variants of Hand Foot and Mouth Disease(HFMD). The symptom is almost the same as its main variant according to the evolution of the strain of enterovirus Coxsackievirus A16(CA16). Although it is less severe than the other variant, the symptom is painful and increases the chance of derma infection which should not be overlooked. According to the simulation, the reproduction number(R0) is estimated to be 5.9 which, relatively close to the endemic of HFMD, occurred in Guangdong , China in 2009[2].

In the perspective of disease spreading, High contact between the infected group and susceptible result in the worst outcome without doubt as the disease spread through the contact with the fluid inside the blister and droplets from sneezing. Considering the result after applying the intervention, at threshold 81 percent which infected the population following the act of isolation or completeness of the isolation.

Thus, the isolation intervention should be strictly applied as soon as the endemic occurs. Educational communication should proceed through the media or social network to make people aware of the disease and guide them to the correct act of the intervention.

Reference

[1] “Kerala Tomato Flu - A Manifestation of Hand Foot and Mouth Disease - PubMed.” *PubMed*, https://pubmed.ncbi.nlm.nih.gov/35980830/. Accessed 25 Sept. 2022.

[2] “Estimating the Basic Reproduction Rate of HFMD Using the Time Series SIR Model in Guangdong, China - PMC.” *PubMed Central (PMC)*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5503211/. Accessed 25 Sept. 2022.