Amath 383 Group Project Proposal Paper

Analysis on SEIR Model for Ebola Transmission in 2013-2016

Group members: Danni Shi, Qiaoxue Liu, Tianning Li

Spring 2019

Abstract

The Ebola Virus Disease (EVD) is an infectious disease with high case fatality and has been a current global health concern. In this project, we will consider the case of the 2013-2016 EVD outbreak in West Africa and build mathematical models based on the "Susceptible, Exposed, Infectious, Recovered" (SEIR) model by separating the "infectious" group into two parts based on symptoms: the early stage (malaria-like) and the advanced stage (including massive bleeding.) With analysis of our model, we will find out the reproduction ratio (R_0) of the EVD in the 2013-2016 outbreak and we will discuss the stability of our model.

1 Introduction

1.1 Background Information

The Ebola Virus Disease (EVD) is a disease in people and nonhuman primates. It is spread from human to human via direct contact with the blood or body fluids (urine, saliva, sweat, feces, vomit, breast milk, and semen) of a person who is sick with or has died from the EVD. In this project, we will be focusing on the Ebola outbreak in 2014. It started in a village in Guinea bordering Guinea, Liberia and Sierra Leone at the end of 2013 and eventually caused more than 28,000 infections and 11,100 deaths by Dec. 2015

in West Africa [1] with an average case fatality of 39.5% the 2013-2016 West Africa outbreak [2], and is considered as the biggest and the most severe EVD outbreak since 1970s before the current outbreak in the Democratic Republic of Congo.

The symptoms may appear from 2 to 21 days after contact with the virus, with an average of 8 to 10 days. The symptoms at the early stages, including fever, headache, fatigue, muscle pain and nausea, are very similar to the ones of more common diseases like typhoid flu and malaria. [3] Later patients would experience unexplained hemorrhage (bleeding or bruising) When used early, basic interventions can significantly improve the chances of survival, although we need to bear in mind that there was no specific treatment for the EVD in 2013-2016. [4]

However, many infected people and their communities did not choose to be hospitalized and treated at the early stages for multiple reasons. Some people were misdiagnosed with malaria. Some did not trust the public health authorities as they warned the local residents that their burial ceremony tradition, including touching the corpse of the dead to show respect, could be dangerous and might spread the disease, which was considered as disrespect to their traditions. Moreover, the weak local public health infrastructure, the feebly conducted surveillance, the poor control of the outbreak all contributed to the spread of the disease.

1.2 Questions of interest

In this project, we are interested in the dynamics of the transmission of the EVD. Since the rate of recovery is significantly higher if the patient is treated at the early stage, and the one at the advanced stage, during which more symptoms specifically for Ebola (such as hemorrhage) would appear, is much lower, we decide to separate patients' status of being infectious into two: the early stage and the advanced stage. We are interested in the dynamics of the infection of the disease when such separation is added to our model. We also hope to find the corresponding reproduction ratio (R_0), which is an important variable in outbreak investigation.

2 Mathematical Model

2.1 Basics: SIR and SEIR Models

2.1.1 SIR

Compartmental models are widely used in mathematical modelling of infectious diseases. The simplest and the most fundamental one would be the "Susceptible, Infectious, Recovered" (SIR) model. [5] We divide the total population (N) into 3 classes: S for the number of susceptible (at risk), I for the number of the infectious population, and R for the number of those who recovered. We also suppose $\frac{\mathrm{d}S}{\mathrm{d}t} + \frac{\mathrm{d}I}{\mathrm{d}t} + \frac{\mathrm{d}R}{\mathrm{d}t} = 0$, $S(t) + I(t) + R(t) = N$. Define β as the per capita infection rate, γ as the recovery rate per capita, $r > 0, a > 0$. A simple SIR model could be

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\beta SI \tag{1}$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI - \gamma I \tag{2}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \gamma I \tag{3}$$

In (1), the infected people are removed from the susceptible group and moved to the infected group in (2). In (3), the recovered group are those who used to be in the infectious group and recovered.

2.1.2 SEIR

Since the EVD has incubation period, that is, there is a period of time before the patient becomes infectious and spread the disease to others after he/she is exposed to the virus, we have to introduce the latent group (people who are infected but not infectious yet or showing explicit symptoms) to our model. So here we must use an SEIR ("Susceptible, Exposed, Infectious, Recovered") model and we denote the latent group with E. [6] Based on the SIR model, we define σ as the latent rate per capita, and a simple SEIR model could be

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\beta SI \tag{4}$$

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \beta SI - \sigma E \tag{5}$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \sigma E - \gamma I \tag{6}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \gamma I \tag{7}$$

In (5), those who were exposed and became infectious are removed from the exposed group and transferred to the infectious group in (6).

2.2 SEIR Model for Ebola Transmission

Now we need to consider the adjustments of SEIR model to the EVD. Here we have $I = I_E + I_L$ with I_E being the group of infectious patients with early-stage symptoms and I_L being the one with advanced-stage symptoms. [7] So $S(t) + E(t) + I_E(t) + I_L(t) + R(t) = N$. We assume that those who recovered will develop antibodies in them and will not rejoin the susceptible group, and all newborns are free of the EVD. So we can have models of [8]

$$\frac{\mathrm{d}S}{\mathrm{d}t} = \delta N - \beta S(I_E + I_L) - \lambda S = \delta N - \beta SI - \lambda S \tag{8}$$

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \beta S(I_E + I_L) - \sigma E - \lambda E = \beta SI - \sigma E - \lambda E \tag{9}$$

$$\frac{\mathrm{d}I_E}{\mathrm{d}t} = \sigma E - \gamma_E[(1-\alpha)I_E] - \alpha I_E - \lambda I_E \tag{10}$$

$$\frac{\mathrm{d}I_L}{\mathrm{d}t} = \gamma_E(1-\alpha)I_E - \gamma_L I_L - \lambda I_L \tag{11}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \gamma_L I_L + \alpha I_E - \lambda R \tag{12}$$

with new notations of

- δ: natural birth rate per capita.
- λ: natural death rate per capita.
- α: rate of hospitalization at the early stage per capita. We assume that hospitalization at the early stage could guarantee recovery.

- γ_E: rate of transferring from the early stage to the advanced stage per capita.
- γ_L: rate of recovery (from the advanced stage) per capita.

In each group, natural deaths occur and are removed from the group. In (8), the newborns are introduced. In (10), a certain proportion (α) of the infectious population at the early stage are hospitalized and treated. We assume that these people are cured and thus removed in I_E and transferred to R in (12). For those who were not hospitalized or treated at the early stage (a proportion of $(1-\alpha)$ of I_E), a proportion (γ_E) of them are transferred to I_L in (11). Here is a diagram summarizes what we think the dynamics could be:

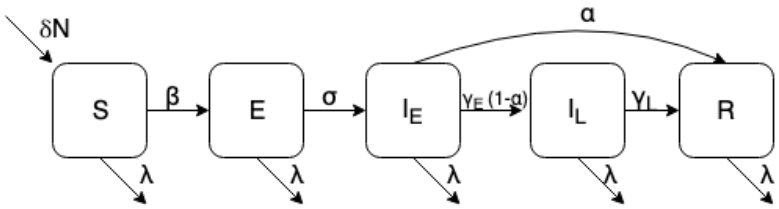

Figure 1: A compartment diagram of our SEIR EVD model with vital dynamics

Note that if we expect the entire population to remain the same during the outbreak, i.e., $\frac{\mathrm{d}N}{\mathrm{d}t} \approx 0$, we expect to have

$$\begin{aligned}\frac{\mathrm{d}N}{\mathrm{d}t} &= (8) + (9) + (10) + (11) + (12) \\ &= \delta N - \lambda(S + E + I_E + I_L + R) = \delta N - \lambda N \approx 0 \\ &\Rightarrow \delta \approx \lambda\end{aligned}$$

3 Analysis

3.1 Equilibrium Points

Here we first want to find the equilibrium points. Set

$$\frac{\mathrm{d}S}{\mathrm{d}t} = 0,\ \frac{\mathrm{d}E}{\mathrm{d}t} = 0,\ \frac{\mathrm{d}I_E}{\mathrm{d}t} = 0,\ \frac{\mathrm{d}I_L}{\mathrm{d}t} = 0,\ \frac{\mathrm{d}R}{\mathrm{d}t} = 0$$

Then we can have

$$(8) = 0 \Rightarrow (\beta I + \lambda)S = \delta N$$

$$S^* = \frac{\delta N}{\beta I + \lambda} \tag{13}$$

$$(8) + (9) = \delta N - \lambda S - \sigma E - \lambda E = 0 + 0$$

$$S^* = \frac{\delta N - (\lambda + \sigma)E}{\lambda} \tag{14}$$

$$(10) = 0 \Rightarrow (\gamma_E(1-\alpha) + \alpha + \lambda)I_E = \sigma E$$

$$I_E^* = \frac{\sigma}{\gamma_E(1-\alpha) + \alpha + \lambda} E \tag{15}$$

$$(11) = 0 \Rightarrow (\gamma_L + \lambda)I_L = \gamma_E(1-\alpha)I_E$$

$$I_L^* = \frac{\gamma_E(1-\alpha)I_E^*}{\alpha + \lambda} = \frac{\gamma_E(1-\alpha)\sigma}{(\alpha+\lambda)[\gamma_E(1-\alpha) + \alpha + \lambda]} E \tag{16}$$

$$(15) + (16) = I_E^* + I_L^* = I^* = \left(\frac{\gamma_E(1-\alpha) + \alpha + \lambda}{\alpha + \lambda} \right) \frac{\sigma}{\gamma_E(1-\alpha) + \alpha + \lambda} E$$

$$I^* = \frac{\sigma}{\alpha + \lambda} E \tag{17}$$

$$(12) = 0 \Rightarrow R^* = \frac{1}{\lambda}(\gamma_L I_L^* + \alpha I_E^*)$$

$$R^* = \frac{1}{\lambda} \left(\gamma_L \frac{\gamma_E(1-\alpha)}{\alpha + \lambda} + \alpha \right) \frac{\sigma}{\gamma_E(1-\alpha) + (\alpha + \lambda)} E \tag{18}$$

So far, S, I_E, I_L, R are all expressed in terms of E, the exposed/latent group, so we can express the equilibrium points as

$$(S^*(E^*), E^*, I_E(E^*), I_L(E^*), R(E^*))$$

Set $(9) = 0$, then plug the previous equations into our system, we can have

$$(9) = 0 \Rightarrow (\sigma + \lambda)E = \beta S I$$

$$E^* = \frac{1}{\sigma + \lambda} \left(\frac{\beta}{\lambda} (\delta N - (\sigma + \lambda)E^*) \cdot \frac{\sigma}{\alpha + \lambda} E^* \right)$$

$$(\sigma + \lambda)E^* = \frac{\beta \delta N \sigma}{\lambda(\alpha + \lambda)} E^* - \frac{\beta \sigma (\sigma + \lambda)}{\lambda(\alpha + \lambda)} E^{*2}$$

Solve the previous equation, the results are

$$E_1^* = 0,\ E_2^* = \frac{\delta N}{\sigma + \lambda} - (\alpha + \lambda)\frac{\lambda}{\beta\sigma} \tag{19}$$

Thus, we can have two fixed points:

$$(S_1^*, E_1^*, I_{E_1}^*, I_{L_1}^*, R_1^*) = (0, 0, 0, 0, 0) \text{ (trivial and boring)} \tag{20}$$

$$(S_2^*, E_2^*, I_{E_2}^*, I_{L_2}^*, R_2^*) = (S^*(E_2^*), E_2^*, I_E(E_2^*), I_L(E_2^*), R(E_2^*)) \tag{21}$$

with E_2^* is as described in (19) and S^*, I_E^*, I_L^*, R^* are as described in (8), (10), (11) and (12) respectively.

3.2 Basic Reproduction Ratio/Number R_0

The basic reproduction ratio/number (R_0) is used to measure the transmission potential of a disease. It is thought of as the number of secondary infections produced by a typical case of an infection in a population that is totally susceptible.[9] (i.e., the average number of people that an infectious patient can transmit the disease to.) It helps us to determine whether or not an infectious disease can spread through a population, so it is considered to be an important variable in outbreak investigation.

When $R_0 < 1$, in the long run, the infectious disease would die out; when $R_0 > 1$, the disease would be spread through the population as the infected population will grow exponentially. The R_0 in the 2013-2016 West Africa Ebola outbreak is believed to be between 1.5 and 2.5. [10]

3.2.1 Jacobian

We here want to use the linear system of differential equations to find R_0. Since we are particularly interest in the groups of people that are infected and can spread infection, we here only focus on the incubation group (E) and the two infected groups (I_E and I_L). From the previous model, define f, g, h

such that

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \beta S(I_E + I_L) - \sigma E - \lambda E = f(E, I_E, I_L)$$
$$\frac{\mathrm{d}I_E}{\mathrm{d}t} = \sigma E - \gamma_E[(1-\alpha)I_E] - \alpha I_E - \lambda I_E = g(E, I_E, I_L)$$
$$\frac{\mathrm{d}I_L}{\mathrm{d}t} = \gamma_E[(1-\alpha)I_E] - \gamma_L I_L - \lambda I_L = h(E, I_E, I_L)$$

Here we will develop linear systems of differential equations to find the R_0.

a) For $E_1^* = 0$, we have J_1

$$J_1 = \begin{pmatrix} \frac{\partial f}{\partial E} & \frac{\partial f}{\partial I_E} & \frac{\partial f}{\partial I_L} \\ \frac{\partial g}{\partial E} & \frac{\partial g}{\partial I_E} & \frac{\partial g}{\partial I_L} \\ \frac{\partial h}{\partial E} & \frac{\partial h}{\partial I_E} & \frac{\partial h}{\partial I_L} \end{pmatrix} = \begin{pmatrix} -(\sigma+\lambda) & \frac{\beta\sigma N}{\lambda} & \frac{\beta\sigma N}{\lambda} \\ \sigma & -\gamma_E(1-\alpha) - (\alpha+\lambda) & 0 \\ 0 & \gamma_E(1-\alpha) & -(\gamma_L+\lambda) \end{pmatrix}$$

b) For $E_2^* = \frac{\delta N}{\sigma+\lambda} - (\alpha+\lambda)\frac{\lambda}{\beta\sigma}$, we have J_2

$$J_2 = \begin{pmatrix} \frac{\partial f}{\partial E} & \frac{\partial f}{\partial I_E} & \frac{\partial f}{\partial I_L} \\ \frac{\partial g}{\partial E} & \frac{\partial g}{\partial I_E} & \frac{\partial g}{\partial I_L} \\ \frac{\partial h}{\partial E} & \frac{\partial h}{\partial I_E} & \frac{\partial h}{\partial I_L} \end{pmatrix} = \begin{pmatrix} -(\sigma+\lambda) & \frac{\beta\delta N - \beta(\lambda+\sigma)E_2^*}{\lambda} & \frac{\beta\delta N - \beta(\lambda+\sigma)E_2^*}{\lambda} \\ \sigma & -\gamma_E(1-\alpha) - (\alpha+\lambda) & 0 \\ 0 & \gamma_E(1-\alpha) & -(\gamma_L+\lambda) \end{pmatrix}$$

3.2.2 Calculating R_0 & Determine Stability

Since both J has the same form, so a would be $a = \frac{\beta\sigma N}{\lambda}$ when $E = E_1 = 0$, and $a = \frac{\beta\delta N - \beta(\lambda+\sigma)E_2}{\lambda}$ when $E = E_2 = \frac{\delta N}{\sigma+\lambda} - (\alpha+\lambda)\frac{\lambda}{\beta\sigma}$. Let $b = \gamma_E(1-\alpha)$. Define two new matrices F and V. F represents the new infections from susceptible, whereas V represents the transfer of infected individuals from one infected class to another. Use the next generation method, we define $J = F - V$, then

$$F = \begin{pmatrix} -(\sigma+\lambda) & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} 0 & -a & -a \\ -\sigma & b-\alpha+\lambda & 0 \\ 0 & -b & \gamma_L+\lambda \end{pmatrix}$$

We can calculate the inverse of V

$$V^{-1} = \begin{pmatrix} \frac{(b-\alpha+\lambda)(\gamma_L+\lambda)}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & \frac{ab+a\gamma_L+a\lambda}{1-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & \frac{ab-a\alpha+a\lambda}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} \\ \frac{\gamma_L\sigma+\lambda\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & 0 & \frac{a\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} \\ \frac{b\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & 0 & -\frac{a\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} -(\sigma+\lambda) & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \cdot \begin{pmatrix} \frac{(b-\alpha+\lambda)(\gamma_L+\lambda)}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & \frac{ab+a\gamma_L+a\lambda}{1-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & \frac{ab-a\alpha+a\lambda}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} \\ \frac{\gamma_L\sigma+\lambda\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & 0 & \frac{a\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} \\ \frac{b\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & 0 & -\frac{a\sigma}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} \end{pmatrix}$$

$$= \begin{pmatrix} \frac{(b-\alpha+\lambda)(\gamma_L+\lambda)(-\lambda-\sigma)}{-ab\sigma-a\gamma_L\sigma-a\lambda\sigma} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

where R_0 is the dominant eigenvalue for matrix FV^{-1}, which is

$$R_0 = \frac{(b-\alpha+\lambda)(\gamma_L+\lambda)(\lambda+\sigma)}{ab\sigma+a\gamma_L\sigma+a\lambda\sigma}$$

- If $R_0 > 1$, then the equilibrium $P^* = (S^*, E^*, I^*, R^*)$ of the virus is obtained and the virus is able to invade the population. The system of (8), (9), (10), (11) and (12) would be unstable. [11]

- If $R_0 < 1$, then the disease free equilibrium $P_0 = (\frac{\delta N}{\lambda}, 0, 0, 0)$of the virus is obtained, which corresponds to the case when the virus dies out (the spread of the outbreak eventually dies out). The system of (8), (9), (10), (11) and (12) would be locally asymptotically stable.

4 Discussion & Improvement

Although we built the modified SEIR model based on the characteristics of Ebola, the effect of some other groups that are not included in our model should not be neglected in the real world. The following are the possible factors we can consider for our model.

4.1 Hospitalization & Treatment

Previously we stated that if the patient was hospitalized at the early stage, he/she would be guaranteed to recover, but it is not always the case in the real world. Let $H(t)$ denote as people go into the hospital.

$$\frac{\mathrm{d}H}{\mathrm{d}t} = \alpha_h I_E - \omega H \tag{22}$$

with new notation of:

- α_h: probability of a person with early stage Ebola that are sent to the hospital.
- ω: rate of people in their early stage of Ebola are treated and recovered in hospital.

4.2 The Chosen One and the Unlucky One

We also have not considered immunity in our model. Previously we assumed that patients who recovered from the EVD can have antibodies built in them, but studies have shown that this only happened to some patients. Let $M(t)$ denote the group of people who are immune to Ebola. M is composed of the group who are congenital immune to Ebola and the group who are cured in the their early stage of Ebola and thus are immune, excluding the group who are unfortunately not immune to Ebola although they are cured in the hospital. Therefore, we have the formula for $\frac{\mathrm{d}M}{\mathrm{d}t}$ as below:

$$\frac{\mathrm{d}M}{\mathrm{d}t} = \theta S + \omega H - cM \tag{23}$$

with new notations of:

- θ: rate of people in the total group that are congenital immune to Ebola (aka. the chosen one.)

- c: rate of people were cured by the hospital, but, unfortunately, they are still not immune to Ebola (aka. the unlucky group.)

4.3 The missing case

The missing cases are the cases which people are infected by the Ebola Virus but they choose not to go to the hospital. It will affected our parameters in the model. Like β, the per capita infection rate will increase and γ_L , the recovery rate per capita will decrease. In this project, we choose to combine both recorded cases and the missing cases. However, the real world has never been nice to us. The current EVD outbreak in the Democratic Republic of Congo has lots of missing cases. The chaotic political situation and people's repulsion to local and international public authorities make the local residents choose not to be treated. In this case, it would not be easy to estimate the impact of missing cases.

5 Conclusion

In this paper, we have introduce the SIR model and SEIR model. According to our analysis, we have two stable points and we got basic reproduction ratio of the disease (R_0) from our model shown as below:

$$R_0 = \frac{(b - \alpha + \lambda)(\gamma_L + \lambda)(\lambda + \sigma)}{ab\sigma + a\gamma_L\sigma + a\lambda\sigma}$$

When $R_0 < 1$, the system would be asymptotically stable and the spread of the disease would die out; when $R_0 > 1$, the system would then be unstable and the infection would spread through the population. In order to estimate the value of R_0, in real world we still have to rely on data to estimate all the parameters.

The dynamics of spread of an infectious disease, especially of a dangerous and complicated one like Ebola, would usually be hard to be summarized as lots of factors are involved and R_0 is determined by many parameters. In the real world, we need to consider even more factors and there is still much room for improvement.

References

[1] World Health Organization (WHO), *Ebola response road map situation report. World Health Organization.* 2015. http://www.who.int/csr/disease/ebola/situation-reports/en/

[2] Shultz, J. M., Espinel, Z., Espinola, M., & Rechkemmer, A. *Distinguishing epidemiological features of the 2013-2016 West Africa Ebola virus disease outbreak* in "Disaster health", 2016, 3(3), 78–88. doi:10.1080/21665044.2016.1228326

[3] Center of Disease Control and Prevention (CDC), *Ebola (Ebola Virus Disease) - Symptoms* in "Viral Hemorrhagic Fevers (VHFs) - Ebola", 2018. https://www.cdc.gov/vhf/ebola/symptoms/

[4] Center of Disease Control and Prevention (CDC), *Ebola (Ebola Virus Disease) - Prevention* in "Viral Hemorrhagic Fevers (VHFs) - Ebola", 2018. https://www.cdc.gov/vhf/ebola/prevention/

[5] Kermack WO & McKendrick AG, *A Contribution to the Mathematical Theory of Epidemics.* Proceedings of the Royal Society A, 1927. 115 (772): 700–721. doi:10.1098/rspa.1927.0118

[6] Anderson RM, May RM: *Infectious Diseases of Humans: dynamics and control*, Oxford University Press; 1991.

[7] Jiang, S., Wang, K., Li, C., Hong, G., Zhang, X., Shan, M., Li, H. and Wang, J. (2017). *Mathematical models for devising the optimal Ebola virus disease eradication.* Journal of Translational Medicine, 15(1).

[8] Rachah, A., Torres, D.F.M., *Analysis, simulation and optimal control of a SEIR model for Ebola virus with demographic effects.* Commun. Fac. Sci. Univ. Ank. Ser. A1 Math. Stat. 67 (2018), no. 1, 179–197 doi:10.1501/Commua1_0000000841

[9] Rothman KJ, Modern Epidemiology, Lippincott Williams & Wilkins, 1998.

[10] Althaus, Christian L. (2014). "Estimating the Reproduction Number of Ebola Virus (EBOV) During the 2014 Outbreak in West Africa". PLoS Currents. 6. doi:10.1371/currents.outbreaks.91afb5e0f279e7f29e7056095255b288

[11] M. Tahir, S. I. A. Shah, G. Zaman, and S. Muhammad, *Ebola virus epidemic disease its modeling and stability analysis required abstain strategies*," "Cogent Biology", vol. 4, no. 1, 2018.