

The Ebola Virus: Factors Affecting the Dynamics of the Disease

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Abstract

We analyze an Ebola epidemic using *Susceptible-Infected-Recovered* (*S-I-R*), deterministic and stochastic models. The models include two stages for the infectious class, a recovery class, and a quarantined class. The stochastic model was analyzed using simulations. We report on factors such as epidemic size, mean time to extinction, and the number of fatalities under a wide set of parameters. An increase in the quarantine rate will reduce the size of an epidemic. However, it will not reduce the mean time to extinction of the epidemic. As you quarantine symptomatic infectives at a high rate, the individuals in the asymptomatic stage of infection will mostly spread the disease. As there is a greater difference between per capita infectivity rates, the epidemic size also increases.

1 The Ebola Virus

1.1 Understanding Viral Hemorrhagic Fevers

Viral Hemorrhagic Fevers (VHF) are characterized by a particular group of illnesses. These illnesses are caused by a distinct family of viruses, a number of which are geographically restricted. Their natural hosts are rodents and arthropods. The illnesses can range from relatively mild to very severe, often causing death[1]. All forms of the disease begin with fevers, head aches, cold sweats and muscle aches. As the disease progresses, complications might occur. These complications include blood clot failure which can result in bleeding from various orifices of the body, vomiting, kidney problems, and shock. The four distinct virus families that cause VHF are filoviruses, arenaviruses, flaviviruses and bunyaviruses[2].

Ebola Hemorrhagic Fever is caused by the Ebola Virus which belongs to the filovirous family (*Filoviridae*). Filoviridae viruses appear thin and filamentous when viewed under an electron microscope. The Ebola virus usually appears as a "b", a "U," or circular shaped organism (see Figure 1).

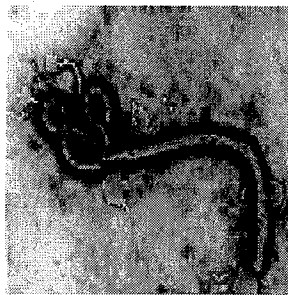
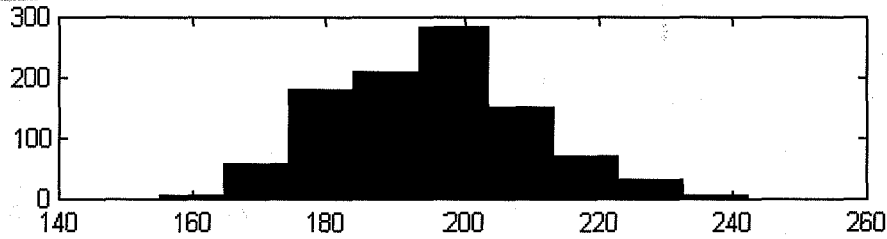


Figure 1: *The Ebola Virus: Taken from the Center for Disease Control and Prevention (CDC) World-Wide Web page. Original photo of the virus was magnified 160,000 times.*

The natural host of the virus is unknown at this point in time. However, there are four known strains of the Ebola Virus which can affect *Homo sapiens* or non-human primates (monkeys and chimpanzees). Each strain has a name that resembles the geographical location at which the virus was first recognized. The outbreaks initially occurred in Zaire, Sudan, Reston. There was an individual in the Ivory-Coast who was infected with this strain, but there was no outbreak. Depending on the strain, this often fatal disease can

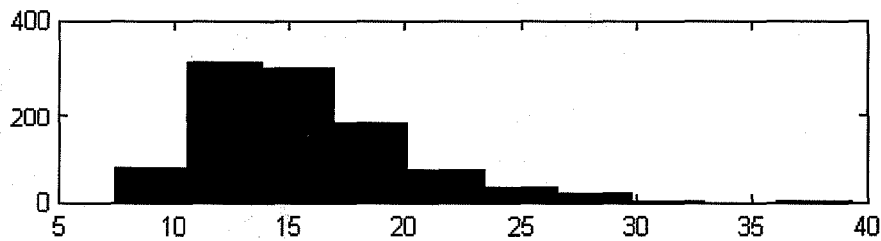
Epidemic Size



Mean: 195.1530

SD: 14.2939

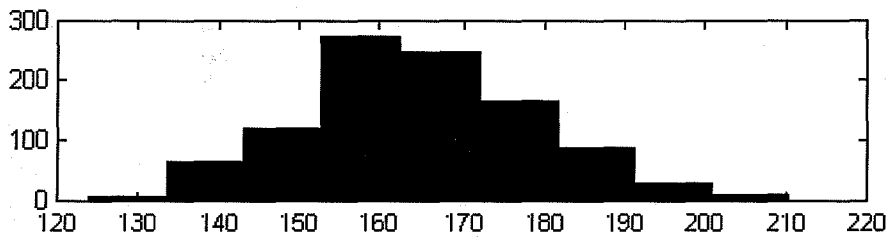
Mean Time to Extinction



Mean: 15.7186

SD: 4.4470

Fatalities



Mean: 164.7350

SD: 14.4445

These histograms correspond with our stochastic simulation data. As you can see, the epidemic size decreases as you increase quarantine. However, the mean time to extinction stays the same.

Epidemic Size				
q		0.5	1	4
$\beta_2 = \frac{2}{3}$	M	251.05	195.51	151.95
	SD	23.57	13.29	6.89
	R_0	0.97	0.70	0.37
$\beta_2 = \frac{5}{3}$	M	510.64	411.61	180.26
	SD	7.20	34.70	11.17
	R_0	2.10	1.42	0.60
$\beta_2 = \frac{10}{3}$	M	524.78	521.77	257.84
	SD	0.50	2.35	24.21
	R_0	3.97	2.60	0.97

Mean Time to Extinction				
q		0.5	1	4
$\beta_2 = \frac{2}{3}$	M	17.56	15.69	14.68
	SD	4.47	4.28	4.19
	R_0	0.97	0.70	0.37
$\beta_2 = \frac{5}{3}$	M	15.91	16.24	15.01
	SD	3.51	4.06	4.54
	R_0	2.10	1.42	0.60
$\beta_2 = \frac{10}{3}$	M	14.01	13.55	14.99
	SD	3.38	3.60	4.56
	R_0	3.97	2.60	0.97

Fatalities				
q		0.5	1	4
$\beta_2 = \frac{2}{3}$	M	215.24	164.97	126.28
	SD	22.53	13.12	8.13
	R_0	0.97	0.70	0.37
$\beta_2 = \frac{5}{3}$	M	444.65	353.58	151.18
	SD	13.00	33.01	12.06
	R_0	2.10	1.42	0.60
$\beta_2 = \frac{10}{3}$	M	458.48	452.91	218.58
	SD	9.98	13.28	22.76
	R_0	3.97	2.60	0.97

kill between 50% and 90% of the people infected. Outbreaks of Ebola hemorrhagic fever usually lead to epidemics as a result of improper handling of infected patients[4].

1.2 Symptoms

Ebola hemorrhagic fever is composed of various symptoms. However, in the early stages of infection, there is an incubation period where the infective is asymptomatic. This incubation period can range from 2 to 14 days after infection. The time that the virus remains in this incubation stage depends on the method of infection. If the virus comes in direct contact with the bloodstream (such as sharing needles with those infected) then the incubation period will be shorter than other less direct forms of contact (such as sneezing on someone). After infection, an individual might experience any combination of the following symptoms: headache, chills, loss of appetite, weakness, muscle ache, fever, sore throat, malaise, and fatigue. As the infection progresses, infectives experience nausea, vomiting, diarrhea, sporadic rashes all over the body, chest pain, uncontrollable blood loss, conjunctivitis (eye inflammation), and death, usually from shock. Other symptoms that occur include internal bleeding, liver failure, and kidney failure[4].

1.3 Treatment

There is no known cure, treatment, or vaccination for the Ebola virus. Researchers have been trying to develop a treatment to prevent the spread of Ebola. However, the host of the virus is unknown, hence, studying the virus for a cure has been very difficult. Presently, the only way to prevent the spread of the virus is to quarantine those that have been infected and inform people who are caring for the infectives about proper sanitation and barrier methods[4]. Quarantine plays an important part in preventing non-infected individuals from exposure to bodily fluids of infected individuals such as vomit, urine, and stool. In fact, the Center for Disease Control publishes documents that advise on proper quarantine measures[1].

1.4 Description of Ebola Subtypes

1.4.1 Ebola-Zaire

Ebola-Zaire is the first documented occurrence of the virus. It is the deadliest of the four Ebola subtypes. This particular strain carries a killing percentage of approximately 90% of those infected. Ebola-Zaire affects both human and non-human primates. In 1976, the first outbreak occurred in Yambuku, Zaire and surrounding areas. At this initial outbreak site, 318 individuals were infected and 280 of those infected died as a result of the virus. There were 38 individuals who survived. In 1995, an epidemic of the virus occurred in Kikwit, Zaire (Democratic Republic of Congo) and spread to surrounding communities. In this incident, 81% of the 318 reported cases resulted in death. In the following year, three more outbreaks of the virus occurred. In Gabon, Africa, two separate outbreaks occurred. During the first outbreak, 57% of the 37 cases reported were deaths due to the virus. In the second incident, which occurred in the Boue area, 75% of the 60 reported cases were deaths due to the virus. The third incident occurred in South Africa in 1996 where a medical professional was infected. However, the only fatality was the nurse who cared for this individual[3].

The primary reason for the spread of the epidemic was the close personal contact between infected individuals and hospital staff. Also poor hospital practices such as the reusage of contaminated needles and syringes added to the spread of the disease[3][4].

1.4.2 Ebola-Sudan

Ebola-Sudan is another Ebola sub-type that is deadly to humans and non-human primates. There were two occurrences of Ebola-Sudan in 1976. The first in Sudan, Africa where there were 284 reported cases. Of those 284 cases, 53% died and 133 of them recovered. The disease was spread through close personal contacts within a hospital facility. The second incident occurred in a single person who accidentally contracted the disease by a contaminated needle. This person survived. Lastly, in 1979, there was a third occurrence in Sudan, Africa. There were only 34 cases reported. Of those 34 cases, 65% died and 12 recovered[3].

1.4.3 Ebola-Reston

According to the Center for Disease Control (CDC), there have been five incidents of the Ebola-Reston virus. The first case was recorded in 1989 in the United States. The virus was discovered in monkeys at quarantine facilities in Virginia, Texas, and Pennsylvania. The monkeys infected with the virus were imported from the Philippines. In this incident, four people became infected with the virus but they did not become ill. In fact, these individuals developed antibodies. The virus reappeared in the facilities in 1990 and four humans developed antibodies, but did not get sick. In 1992, monkeys infected with Ebola-Reston were imported into the United States from a quarantine facility in Sienna, Italy. However, no humans were infected with the virus. In 1996, infected monkeys imported from the Philippines arrived at a quarantine site in Alice, Texas. Again, no humans were infected. This was also the case in the latest event that occurred in the Philippines in 1996. The virus was identified in monkeys at an export facility[3]. Of all the Ebola-Reston cases, there have been no human deaths or cases of clinical illness due to the virus. However, researchers have not concluded that humans are immune from the virus as further research is necessary[4].

1.4.4 Ebola-Ivory Coast (Tai)

The only case of the Ebola-Ivory Coast strain was documented in 1994. A scientist in the Ivory Coast became ill after performing an autopsy on a chimp. He was later treated and eventually recovered[4].

1.4.5 Purpose

We are interested in how quarantine, barrier methods used by hospitals and clinic personnel to prevent the disease from spreading, affect the spread of an epidemic. Also, in looking at two different stages of infection, how do individuals in the asymptomatic stage and individuals in the symptomatic stage affect the epidemic. We will use deterministic and stochastic models to study the behavior of an Ebola epidemic.

2 The Model

The model is represented by the following diagram:

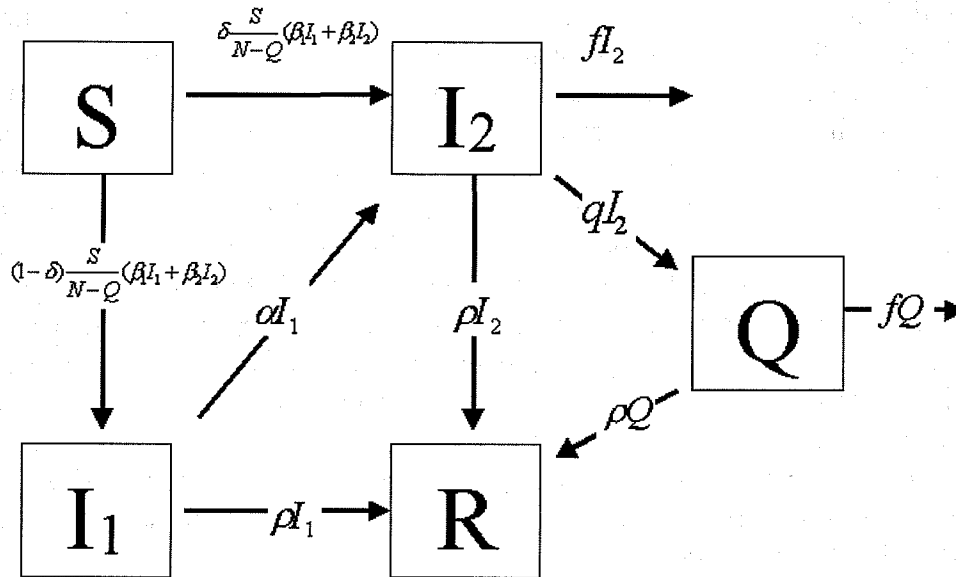


Figure 2: *The transition diagram.*

$$N = S + I_1 + I_2 + Q + R$$

where:

N = total population

S = susceptible individuals

I_1 = infectious individuals with few or no symptoms

I_2 = infectious individuals with severe symptoms

Q = quarantined individuals

R = recovered individuals

The parameters are as follows:

δ = proportion of infections which lead directly to the symptomatic stage

$(1 - \delta)$ = proportion of infections which lead to the asymptomatic stage

α = rate of infection development from (I_1) to severe symptoms (I_2)

β_1 = per capita infectivity rate for asymptomatic infectives

β_2 = per capita infectivity rate for symptomatic infectives

f = fatality rate

q = quarantine rate

ρ = recovery rate

The system of differential equations that govern our model are as follows:

$$\frac{dS}{dt} = \frac{-S}{N - Q} (\beta_1 I_1 + \beta_2 I_2) \quad (1)$$

$$\frac{dI_1}{dt} = (1 - \delta) \frac{S}{N - Q} (\beta_1 I_1 + \beta_2 I_2) - \alpha I_1 - \rho I_1 \quad (2)$$

$$\frac{dI_2}{dt} = \delta \frac{S}{N - Q} (\beta_1 I_1 + \beta_2 I_2) - (q + f + \rho) I_2 + \alpha I_1 \quad (3)$$

$$\frac{dQ}{dt} = q I_2 - f Q - \rho Q \quad (4)$$

$$\frac{dR}{dt} = \rho (I_1 + I_2 + Q) \quad (5)$$

Note: Our model does not include any demographics that are unrelated to the disease state. There are no births, natural deaths or migration.

3 Stability Analysis

In order to determine the behavior of the epidemic, we must linearize the system (1)-(5) at the disease free equilibrium point, $(S,0,0,0,R)$, where S and R are arbitrary. There is no endemic equilibrium because there are no natural births or deaths in our system, as previously stated. People who leave the susceptible class are not replaced. R_0 is the number of people that an average infective person can infect, out of a susceptible population. It is of major importance to determine R_0 for our system of differential equations because we want to know how the number of infected individuals affect the dynamics of Ebola.

R_0 is found using the eigenvalues of the Jacobian of our system of equations. R_0 is a quantity such that when $R_0 < 1$ the real parts of all the eigenvalues of the Jacobian matrix are negative.

When we look at the Jacobian of the 5x5 matrix associated with our system of differential equations we get two eigenvalues that are both equal to zero. When we have eigenvalues that are equal to zero, no conclusions can be drawn and the linearization fails. Therefore, we only look at disease related variables and we get a 3x3 matrix. Clearly, we see that one of the eigenvalues is $-(f + \rho)$, a negative eigenvalue. Hence, we are able to reduce the Jacobian of the 3x3 matrix to a 2x2 matrix. We calculate the R_0 from the following matrix at $(S,0,0,0,R)$ using the determinant and trace:

$$\begin{pmatrix} (1 - \delta)\beta_1 - \alpha - \rho & (1 - \delta)\beta_2 \\ \alpha + \delta\beta_1 & \delta\beta_2 - (f + q + \rho) \end{pmatrix}$$

We are not able to determine any local stability due to the fact that two eigenvalues are always 0, but we can use R_0 to see if we get an epidemic or not.

The determinant is:

$$[(1 - \delta)\beta_1 - (\alpha + \rho)][\delta\beta_2 - (f + q + \rho)] - (\alpha + \delta\beta_1)(1 - \delta)\beta_2.$$

The trace is:

$$(1 - \delta)\beta_1 - \alpha - \rho + \delta\beta_2 - (f + q + \rho).$$

And our R_0 is:

$$R_0 = \left(\frac{1}{\alpha + \rho}\right)\beta_1(1 - \delta) + \left[\delta + \frac{\alpha}{\alpha + \rho}(1 - \delta)\right]\beta_2\left(\frac{1}{f + q + \rho}\right).$$

Now we'll show what R_0 means biologically. A person in I_1 infects others at rate of β_1 , leaves I_1 at a rate of $\alpha + \rho$. On average a person stays in I_1 an average time of $\frac{1}{\alpha + \rho}$. A proportion of $(1 - \delta)$ of all people that become infected go through I_1 . So the overall contribution to R_0 from the I_1 stage is $\frac{1}{\alpha + \rho}\beta_1(1 - \delta)$.

A person in I_2 infects others at rate of β_2 , leaves I_2 at a rate of $f + q + \rho$. So a person stays in I_2 an average time of $\frac{1}{f + q + \rho}$. A proportion δ of all initial infectives and $\frac{\alpha}{\alpha + \rho}$ of I_1 infectives, go through I_2 . So the contribution to R_0 from the I_2 class is $[\delta + \frac{\alpha}{\alpha + \rho}(1 - \delta)]\beta_2\frac{1}{f + q + \rho}$.

This gives us the same value of R_0 as the one that we calculated from the Jacobian of our system of equations if

$$R_0 = \left(\frac{1}{\alpha + \rho}\right)\beta_1(1 - \delta) + \left[\delta + \frac{\alpha}{\alpha + \rho}(1 - \delta)\right]\beta_2\left(\frac{1}{f + q + \rho}\right) < 1,$$

then the two terms must each be less than 1.

Thus

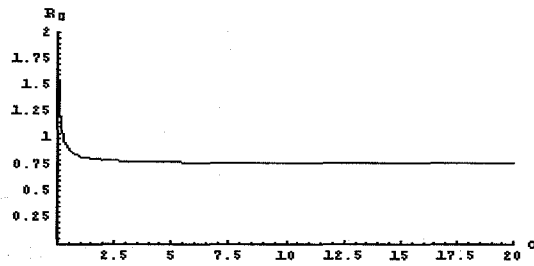
$$(1 - \delta)\beta_1 < \alpha + \rho$$

and

$$\delta\beta_2 < (f + q + \rho).$$

Looking back at our trace:

$$(1 - \delta)\beta_1 - \alpha - \rho + \delta\beta_2 - (f + q + \rho) < 0$$



Example C: The value of β_2 is 3.33.
The value of q is 4.

Figure 4: R_0 vs. α

disease. Also they will be sent into quarantine faster. Thus, reducing the number of susceptibles that become infected. As α decreases, the lower boundary of R_0 approaches and becomes greater than 1.

So, if someone were to vaccinate or provide treatment that would decrease the rate of α to a proportion of a population that is not infected, then we would have a higher chance of an occurrence of an epidemic. We calculated the value of α for which R_0 is equal to 1.

$$R_0(\alpha) = 1$$

$$\alpha = 0.28$$

Which means that on average, the maximum amount of time an individual should remain in I_1 is about three and a half days.

3.1 Stochastic Simulations

Since our model is an attempt to describe the behavior of the Ebola virus in a given population, it is important to examine each of the classes as time progresses, and make comparisons. A good approach to this is the use of computer simulations. Using a computer program(see appendix), we are able to study how the different classes are affected when the disease enters the system. Before running the simulations, we must first assign values to our parameters. The important parameters were varied, while the others were kept fixed. We had several extended discussions on what the range of

the values should be and arrived at the following conclusions.

Based on information from the CDC and the World Health Organization (WHO), we deduced the value of the fatality rate to be approximately:

$$f = \frac{1}{3} = 0.33 \quad (7)$$

which means that on average, it will take a person (3) days to die. Furthermore, the virus has the capacity to kill between 50% and 90% of the infected individuals. An infected individual can either recover or die, so we solve for the recovery rate using the following equation:

$$\frac{f}{f + \rho} = 0.9. \quad (8)$$

Therefore, $\rho = 0.037$.

We also deduced that there is a higher probability that susceptible individuals (S) will move into the (I_2) class, rather than moving into the (I_1) class. From this we approximated $\delta = 0.75$

From our observations we noted that 90% of the individuals in (I_1) move into (I_2), while the remaining 10% recover.

This number is denoted by the following equation:

$$\frac{\alpha}{\alpha + \rho} = 0.9. \quad (9)$$

We can solve for (α) which is the average rate, per days, an individual will remain in the I_1 class before being removed to the I_2 class. We obtain

$$\alpha = \frac{1}{3}. \quad (10)$$

Quarantine and other barrier methods are policies that are commonly used to prevent further spread of the Ebola virus. We will vary the quarantine

rate to determine whether or not it will affect the behavior of the virus in a given population. These are a range of values for (q) that we decided to test:

$$q = .5, 1, 4. \quad (11)$$

We assume that $\beta_1 < \beta_2$ because people in (I_2) are more infectious than people in (I_1). Thus a rate of one-third was chosen to show that one person gets infected by an individual from (I_1) every three days. That is,

$$\beta_1 = 0.33. \quad (12)$$

Based on our assumptions above, β_2 should be represented as a multiple of β_1 . Therefore $\beta_2 = k\beta_1$ where $k = 2, 5, 10$. Hence:

$$\beta_2 = \frac{2}{3}, \frac{5}{3}, \frac{10}{3}. \quad (13)$$

4 Results and Discussion

According to our deterministic graphs, it would be disastrous if a population were given a vaccine or drug that would decrease the α rate. We have seen that as α decreases the value of R_0 increases. We calculated that the maximum amount of time that a person should remain in I_1 should be, on average, about three and a half days. If on average, individuals are spending a longer time in the I_1 stage then we will have an epidemic.

We also plotted the graph of R_0 as a function of q and we saw the behavior of R_0 as quarantine increased. Again we noted that as we increased quarantine, R_0 would decrease. We calculated that on average, the maximum amount of time it would take to quarantine someone, if we would like to stop an epidemic, is about twelve hours.

The I_1 class is very important in our model. At a high rate of quarantine, we are able to stop the virus from spreading within the I_2 class but not from the I_1 class. So if the I_1 class is very large, we can have an epidemic even at a high quarantine rate. Unfortunately, it is very difficult to diagnose the individuals in I_1 as these individuals are in the asymptomatic stage.

The difference between β_1 and β_2 has a great effect on the epidemic size. The epidemic size changes as β_2 changes. That is, the higher the rate of infection of individuals in I_2 , the larger the epidemic. Therefore it's important to quarantine these individuals at a high rate to help reduce the epidemic

size.

When we increase the quarantine rate q , the epidemic size decreases significantly. Even though we increased the quarantine rate, this has no effect on the latency of the epidemic, it lasted approximately the same amount of time. When we increased the quarantine rate, less people died. In conclusion, if the infectious rate of people in I_2 is very large, then no matter how high the rate of quarantine the epidemic size will remain the same.

5 Acknowledgements

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6 Resources

Center for Disease Control and Prevention (C.D.C) World-Wide Web pages

1. <http://www.cdc.gov/wonder/prevgvid/m0037085/entire.htm>
2. <http://www.cdc.gov/ncidod/publications/brochures/ebolainf.htm>
3. <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebotabl.htm>

4. <http://www.cdc.gov/ncidod/vir/fur/ebola528.htm>

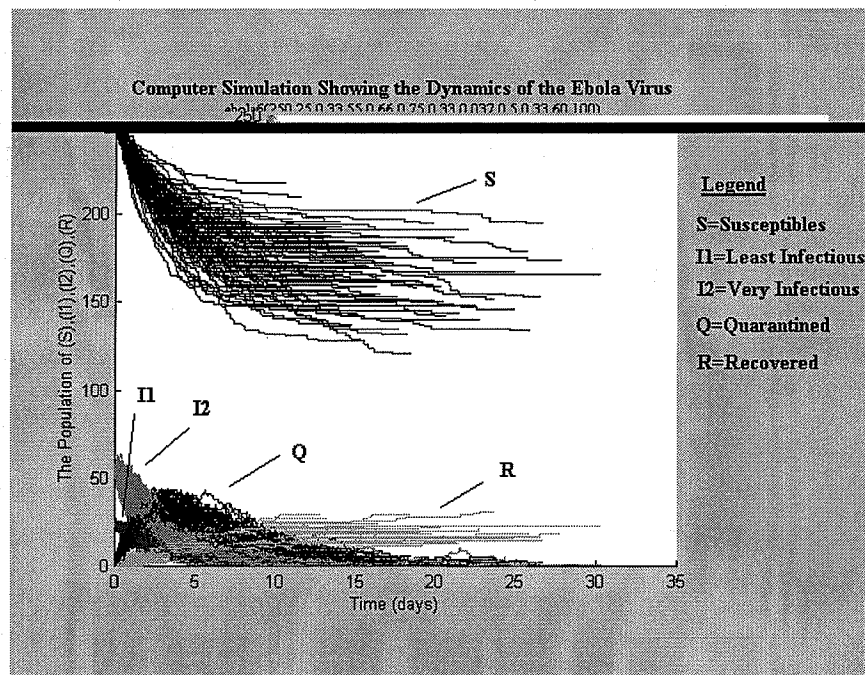
5. <http://www.cdc.gov/ncidod/EID/vol1no3/sanchez.htm>

World Health Organization (WHO) World-Wide Web page

6. <http://www.who.int/emc/diseases/ebola/eboladata.html>

7 Appendix

7.1 Computer Simulations



7.2 Computer Algorithm

```
function initrnd
% Initrnd.m
% seed the random number generator
rand('state',sum(100*clock));

function eventtype=wheel(eventlist)
% eventtype=wheel(eventlist)
% returns the type of event from list of rates
picker=cumsum(eventlist)/sum(eventlist);
eventtype=sum(picker<rand)+1;

function ebola6(s0,i1,b1,i2,b2,tran,sick,r,q,f,T,sim)
% ebola6(s0,i1,b1,i2,b2,tran,sick,r,q,f,T,sim)
% Simulates a simple SIIQR model
% s0    initial suscep. pop.
% i1    initial infected w/o symptoms
% b1    infectious coefficient rate
% i2    initial infected w/symptoms
% b2    infectious coefficient w/symptoms
% tran  rate from S to I1
% sick  rate at which infected becomes very infectious
% r     recovery rate
% q     quarantine rate
% f     fatality rate
% T     is max time
% sim   max number of simulations

tic;
initrnd;

figure(1); %clear figures
clf;
figure(2);
clf;
hold off;
```

```

for simul = 1:sim
    S=s0; % initial value
    I=i1;
    I2=i2;
    Re=0;
    Qt=0;
    t=0; % initial time

    %initial population at start of epidemic for given simulation
    N0=s0+i1+i2+Re+Qt;    Nplot=[S,t,I,I2,Re,Qt];
    while (t<T) & (I+I2>0);
        N=S+I+I2+Re+Qt;
        %finds next event time
        nextt=-log(rand)/(((1-tran)*(b1*S*I/(N-Qt)))+
(tran*(b2*S*I2/(N-Qt)))+(sick*I)+(r*I)+
(q*I2)+(f*I2)+(r*I2)+(r*Qt)+(f*Qt));
        t=t+nextt; %calculate next time
        %event doesnt occur til t, N rem. cons. til t.
        Nplot=[Nplot; [S,t,I,I2,Re,Qt]];

        event=wheel([(1-tran)*b1*S*I/(N-Qt),tran*b2*S*I2/(N-Qt),
sick*I,r*I,q*I2,f*I2,r*I2,r*Qt,f*Qt]); %choose event
        if event==1
            S=S-1;
            I=I+1; %infection
        elseif event==2
            S=S-1;
            I2=I2+1; %recovery
        elseif event==3
            I=I-1;
            I2=I2+1;
        elseif event==4
            I=I-1;
            Re=Re+1;
        elseif event==5
            I2=I2-1;
            Qt=Qt+1;
        elseif event==6

```

```

        I2=I2-1;
    elseif event==7
        I2=I2-1;
        Re=Re+1;
    elseif event==8
        Qt=Qt-1;
        Re=Re+1;
    elseif event==9
        Qt=Qt-1;
    end
    Nplot=[Nplot;[S,t,I,I2,Re,Qt]]; %next point
    [simul,t]; %displays the time, semicolon to turn off

    %plot the total epidemic size, succceptibles, recovered and quarantined
    %after every simulation to get a matrix
    A(simul,:)= [NO-S,S,t,Qt,NO-N,Re];
end

%* for deterministic model comparison *%
figure(1) % this figure will hold the time plots
hold on; %superimpose time plots
plot(Nplot(:,2),Nplot(:,1)); %plot suceptibles with a blue line
plot(Nplot(:,2),Nplot(:,3), 'r-'); %plot infecteds(I1) with a red line
plot(Nplot(:,2),Nplot(:,4), 'g-'); %plot infecteds(I2) with a green line
plot(Nplot(:,2),Nplot(:,5), 'c-'); %plots recovered with a cyan line
plot(Nplot(:,2),Nplot(:,6), 'k-'); %plots quarantined with a black line
title('Blue=(S), Red=(I1), Green=(I2), Black=(Q)')
ylabel('The Population of (S),(I1),(I2),(Q),(R)')
xlabel('Time (days)')
zlabel('test')
if toc >5
    [simul,t] %displays the, time semicolon to turn off
    tic;
end;
end

%* for deterministic model comparison *%
if sim > 1 %only draw the histogram if there is more than 1 simulation

```

```

figure(2);
hold off; %erases any previous histograms
figure(2);
%title('Distribution of the population')
%title('Epidemic Size, Susceptibles, Mean time to Extinction')
subplot(3,1,1)
hist(A(:,1));
subplot(3,1,2)
hist(A(:,2));
subplot(3,1,3)
hist(A(:,3));

figure(3);
%title('Distribution of the population')
%title('Quarantined, Fatalities, Recovered')
hold off; %erases any previous histograms
figure(3);
subplot(3,1,1)
hist(A(:,4));
subplot(3,1,2)
hist(A(:,5));
subplot(3,1,3)
hist(A(:,6));
end
Meanx1 = [mean(A(:,1)),mean(A(:,3)),mean(A(:,5))]
Stdx1 = [std(A(:,1)),std(A(:,3)),std(A(:,5))]

```