The Potential Impact of a Prophylactic Vaccine for Ebola in West Africa

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Abstract

The 2014 outbreak of *ebolavirus* disease (EVD) in West Africa has been multinational and of an unprecedented scale, primarily affecting the countries of Guinea, Liberia, and Sierra Leone. One of the qualities that makes EVD of high public concern is its potential for extremely high mortality rates (up to 90%). A prophylactic vaccine for the *ebolavirus* has been developed, and preliminary results are promising, showing near perfect efficacy. We have developed an ordinary differential equations model which simulates an EVD epidemic and takes into account (1) transmission through contact with infectious EVD individuals and deceased EVD bodies, (2) the heterogeneity of an individual's risk of becoming infected with EVD, and (3) the increased survivability of infected EVD patients through increases in the number of healthcare workers available in the population. Using parameter values which closely simulate the dynamics of the 2014 outbreak in West Africa, we utilize our model to predict the potential impact of a prophylactic vaccine for the *ebolavirus* in Sierra Leone, West Africa. By running model simulations which simulate various vaccination strategies, we discovered that the number of cumulative infected individuals is most sensitive to the parameter α, the proportion of Exposed individuals entering the hospital.

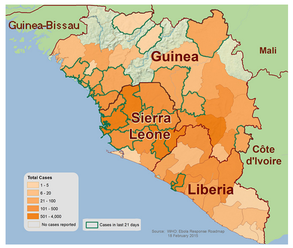
Motivation

Since its 1976 discovery in the country of Zaire (now the Democratic Republic of the Congo), four primary strains of the Ebola virus have been identified with the most deadly strain being the *Zaire ebolavirus* (current outbreak strain). The virus is only transmitted through direct contact, and once infected, an individual may experience symptoms including fever, vomiting, hemorrhagic bleeding, and death. The current outbreak of EVD is located in West Africa and began in January 2014. It is the largest outbreak of EVD to date, affecting multiple countries worldwide. No licensed Ebola virus vaccines are currently available; therefore, researchers are exploring new vaccine strategies. In light of this search for a vaccine, we apply a prophylactic vaccination component to a modified *SEIR* mathematical model. The purpose of this model is to identify the minimum effectiveness of a prophylactic vaccine in order to adequately curb an outbreak of EVD.

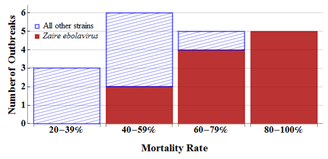
Current EVD Outbreak Statistics

Country	Total Cases	Total Deaths	Mortality Rate (%)
Sierra Leone	14,124	3,956	28.0
Liberia	10,678	4,810	45.1
Guinea	3,814	2,544	66.7
Nigeria	20	8	40.0
Mali	8	6	75.0
United States	4	1	25.0
Senegal	1	0	0
Spain	1	0	0
United Kingdom	1	0	0

Data current as of April 13, 2016.



Map of countries most affected by EVD in West Africa: Sierra Leone, Guinea, and Liberia.



Histogram of mortality rates for the 19 outbreaks of EVD that have had more than 5 reported cases (excluding the 2014 West Africa Outbreak); outbreaks of Zaire ebolavirus are shown in red while all other outbreaks are shown in blue.

Key Model Assumptions

- Individuals who recover are still considered to be infectious for up to 5 months.
- Individuals who recover cannot become infected for at least 10 years.
- Survival rate of infectious individuals in hospitals increases as the number of healthcare workers increases.
- We assume $t = 0$ occurs 30 days before the first reported cumulative deaths and cumulative infections data.
- We assume individuals in R_I will not die from the *Ebolavirus*.

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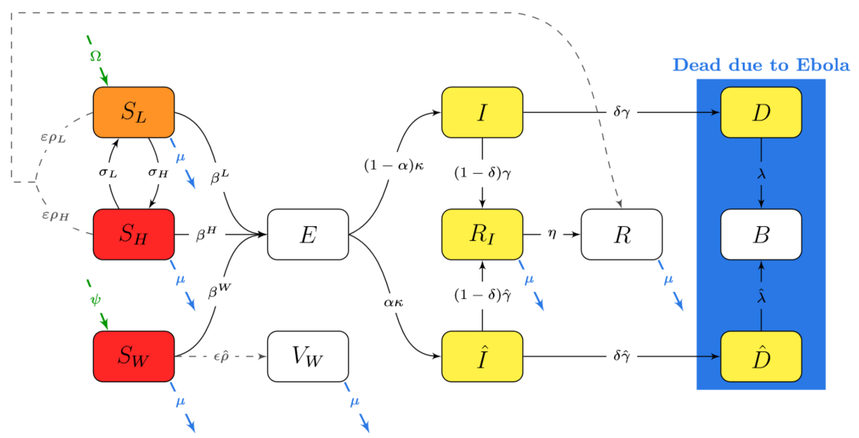
Model



Flow diagram of model given below. Shaded compartments indicate high risk of exposure (red), low risk of exposure (orange), and ability to transmit EVD (yellow). Green arrows indicate movement into the population, blue arrows indicate background death, and dashed line arrow indicate vaccination. The state variables are described as follows: low susceptible (S_L), high susceptible (S_H), healthcare workers (HCW) (S_W), exposed (E), infected (I), infected in hospital (I_H), recovered and infectious (R_I), recovered (R), vaccinated HCW (V_W), dead (D), dead in hospital (D_H), buried (B).

A Population Model of Ebola

$$S_L'(t) = \Omega - \frac{(\beta_1^L I + \beta_2^L D + \beta_3 R_I)S_L}{N} - \varepsilon\rho_L S_L + \sigma_L S_H - \sigma_H \frac{I+\hat{I}+D+\hat{D}}{N} S_L - \mu S_L$$

$$S_H'(t) = -\frac{(\beta_1^H I + \beta_2^H D)S_H}{N} - \varepsilon\rho_H S_H + \sigma_H \frac{I+\hat{I}+D+\hat{D}}{N} S_L - \sigma_L S_H - \mu S_H$$

$$S_W'(t) = \psi(\phi + I + \hat{I} + D + \hat{D}) - \frac{(\beta_1^W \hat{I} + \beta_2^W \hat{D})S_W}{N} - \varepsilon\hat{\rho} S_W - \mu S_W$$

$$E'(t) = \frac{(\beta_1^H I + \beta_2^H D)S_H + (\beta_1^L I + \beta_2^L D + \beta_3 R_I)S_L + (\beta_1^W \hat{I} + \beta_2^W \hat{D})S_W}{N} - \kappa E$$

$$R_I'(t) = \gamma(1-\delta)I + \hat{\gamma}\left(1 - \delta\nu\frac{\phi}{\phi + S_W + V_W}\right)\hat{I} - \eta R_I - \mu R_I$$

$$R'(t) = \varepsilon(\rho_H S_H + \rho_L S_L) + \eta R_I - \mu R$$

$$I'(t) = \kappa(1-\alpha)E - \gamma I$$

$$\hat{I}'(t) = \kappa\alpha E - \hat{\gamma}\hat{I}$$

$$D'(t) = \gamma\delta I - \lambda D$$

$$\hat{D}'(t) = \hat{\gamma}\left(\delta\nu\frac{\phi}{\phi + S_W + V_W}\right)\hat{I} - \hat{\lambda}\hat{D}$$

$$B'(t) = \lambda D + \hat{\lambda}\hat{D}$$

$$V_W'(t) = \varepsilon\hat{\rho} S_W - \mu V_W$$

Parameters

	Parameter	Units	Value	Description
Fitted Parameters	β_1^H	$1/days$	0.651*	transmission rate from infectious individuals to high risk susceptible individuals
	β_1^L	$1/days$	0.471*	transmission rate from infectious individuals to low risk susceptible individuals
	β_1^W	$1/days$	0.163*	transmission rate from infectious individuals to susceptible healthcare workers
	β_2^H	$1/days$	0.294*	transmission rate from deceased individuals to high risk susceptible individuals
	β_2^L	$1/days$	0.436*	transmission rate from deceased individuals to low risk susceptible individuals
	β_2^W	$1/days$	0.720*	transmission rate from deceased individuals to susceptible healthcare workers
	β_3	$1/days$	0.000765*	transmission rate from recovering, still infectious individuals to low risk individuals
	α	—	0.407*	proportion of symptomatic individuals who go to the hospital
	ν	—	0.691*	scaling constant representing effectiveness of healthcare workers in reducing EVD death rate
Vax	ϵ	—	1	proportion of individuals in whom the vaccine is effective
	ρ	—	Varies	proportion of general susceptible population ($S_H + S_L$) who get vaccinated per year
	$\hat{\rho}$	—	Varies	proportion of healthcare workers (S_W) who get vaccinated per year
	ψ	$1/days$	Varies	migration rate of healthcare workers into the population
	μ	$1/days$	$^{11.03}/_{(1,000)(365)}$	natural death rate per day per 1,000 individuals
	Ω	$people/days$	$^{37.4}/_{(1,000)(365)}$	natural birth rate per day per 1,000 individuals
	κ	$1/days$	$^1/_{5.5}$	rate at which individuals become symptomatic and infectious
	$1/\gamma$	$days$	9	infectious period of individuals who are not in hospitals
	$1/\hat{\gamma}$	$days$	7	infectious period of individuals who are in hospitals
	δ	—	0.73	proportion of individuals who die from Ebola
	ϕ	$people$	0.00039N(0)	number of healthcare workers in the population prior to outbreak
	λ	$1/days$	$^1/_5$	burial rate of deceased individuals who were not in hospitals
	$\hat{\lambda}$	$1/days$	$^1/_2$	burial rate of deceased individuals who were in hospitals
	η	$1/days$	$^1/_{150}$	rate at which recovering and still infectious individuals become non-infectious
	σ_H	$1/days$	κ	rate at which individuals move from low risk to high risk susceptible populations
	σ_L	$1/days$	$1/(^1/_\gamma + ^1/_\lambda)$	rate at which individuals move from high risk to low risk susceptible populations

*Fitted values from the first time period which were used for simulations in the table comparing different vaccination strategies.

Comparing Different Vaccination Strategies

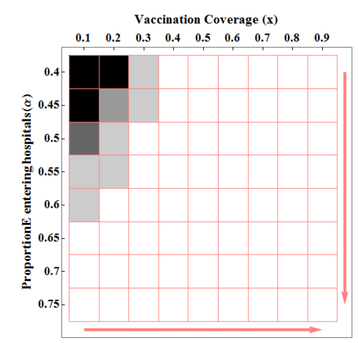
Effect of vaccination prior to an initial outbreak (1 infected). Vaccination coverage of healthcare workers is 0% when $x = 0$ and 95% otherwise. Value given parenthetically to the right of total cases reports the death rate. The last three columns display the results of a ring vaccination strategy implemented after the outbreak begins.

x	Vax prior to $t = 0$: $\rho_L = \rho_H = 0$, $\hat{\rho} = 0$			Vax prior to $t = 0$ & for $t > 0$: $\rho_L = \rho_H = {}^{0.3}/_{365}$, $\hat{\rho} = {}^{0.9}/_{365}$			Vax prior to $t = 0$ & for $t > 0$: $\rho_L = {}^{0.01}/_{365}$, $\rho_H = {}^{0.95}/_{21}$, $\hat{\rho} = {}^{0.99}/_{7}$		
	CI	t^*	PI	CI	t^*	PI	CI	t^*	PI
0	4,156,370	495	292,226	3,743,965	516	235,677	2,650,846	492	157,935
0.10	3,064,971	648	150,417	2,506,362	694	101,171	1,853,742	644	76,661
0.20	1,866,043	974	52,428	1,026,659	1138	17,969	1,040,091	987	23,869
0.25	1,256,742	1339	23,007	162,871	1639	1257	605,607	1409	8322
0.30	660,879	2241	6223	1201	1060	8	91,633	2540	439
0.35	94,409	8894	153	70	0	1	158	0	1
0.40	26	0	1	20	0	1	23	0	1
0.50	7	0	1	7	0	1	7	0	1
0.60	4	0	1	4	0	1	4	0	1
0.70	2	0	1	2	0	1	2	0	1
0.80	2	0	1	2	0	1	2	0	1
0.90	1	0	1	1	0	1	1	0	1

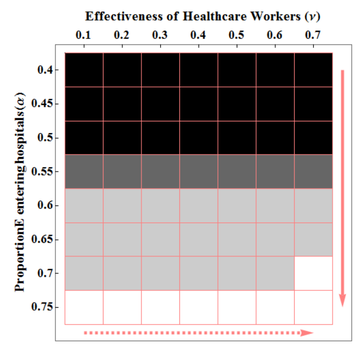
t^* is the day at which the peak number of cases occurs; CI represents cumulative infections calculated once $I(t) + \hat{I}(t) < 1$; PI represents the number of infections on the peak day, i.e. $I(t^*) + \hat{I}(t^*)$

Sensitivity Analysis of Ring Vaccination Strategy

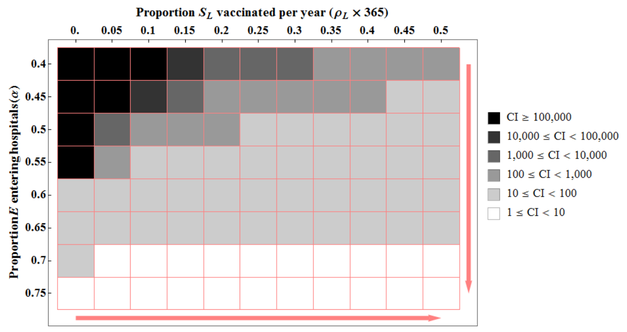
Matrix plots displaying the sensitivity of the parameters to the cumulative number of infected individuals (CI) during a ring vaccination scenario with $\epsilon = 1$, $\rho_H = {}^{0.95}/_{21}$, and $\rho_W = {}^{0.99}/_{7}$.



$\nu = 0.691$, $\rho_L = {}^{0.01}/_{365}$



$x = 0$, $\rho_L = {}^{0.01}/_{365}$



$x = 0$, $\nu = 0.691$

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