

A Quantitative Assessment of Dynamic Intervention-Capacity Effectiveness in the 2014 Ebola Epidemic

Willem L. Auping (HCSS)*, Erik Pruyt (NIAS & TU Delft), Jan H. Kwakkel (TU Delft), Michel Rademaker (HCSS)

*Corresponding author: willemauping@HCSS.nl

Abstract

Background: The current outbreak of the Ebola Virus (EBOV) is characterized by inadequate intervention capacities. In this theoretical paper, we research what the influence of limitations in the intervention capacity are on the effective reproduction number, and what the effectiveness would be of a more proactive approach in expanding the intervention capacities.

Methodology: We use a transmission model extended with dynamical intervention capacities of isolation, health workers, tracing officers, and eventually vaccines. We generate a set of plausible scenarios explaining the current reported Ebola Virus Disease (EVD) cases taking into account a bandwidth for potential underreporting. We use these scenarios to test the effectiveness of a more proactive approach in extending intervention capacities.

Results and conclusions: We show that a reactive approach in extending intervention capacities leads to under-capacity for isolating EVD cases. This under-capacity can lead to a significant increase in the effective reproduction number, leading to faster transmission of EBOV. A more proactive approach, which takes into account development delays of capacities, the doubling time of the disease, and the factor of potential underreporting of the number of cases, helps in any scenario in limiting the total number of EVD cases and deaths.

Keywords: Ebola Virus Disease, Intervention capacity, Reproduction number, Scenario Discovery

Introduction

The 2014 outbreak of Ebola Virus (EBOV) and, consequently, Ebola Virus Disease (EVD) in Liberia, Sierra Leone, Guinea, Senegal, Mali, Nigeria, Spain, and the United States of America^{1,2} is by far the largest observed to date;³ The number of cases and deaths outnumbers the sum of all previous outbreaks of EVD. The outbreak distinguishes itself from earlier

outbreaks by occurring in densely populated urban areas.³ Earlier outbreaks took place in rural or otherwise sparsely populated areas.⁴⁻¹²

Dynamic transmission models can be used for intervention capacity planning for epidemics like the 2014 EVD epidemic. These models have been used for estimating the reproduction number of Ebola, and projecting the future development of the epidemic.^{3,13,14} However, projecting the dynamics of EBOV is complicated by the uncertainty about many input factors.¹⁵ Examples include the case fatality ratio,¹⁶ and the basic reproduction number R_0 .^{3,17,18} Further, the actual number of cases during this epidemic is believed to be considerably higher than the reported number of cases,¹⁹ since the infrastructure to diagnose new cases and identify contamination epicenters is insufficient, as is demonstrated by the continued spreading of the disease.

When EBOV was spreading exponentially, medical staff, hospitals, isolation facilities, and tracing officers were trying to limit the further spreading of the virus, and an effort was started to develop Ebola vaccines and medication as quickly as possible. Therefore, it makes sense to incorporate these intervention capacities in transmission models aimed at projecting the future development of the epidemic. For example, Bachinsky & Nizolenko combine a SEIR model with capacities.²⁰ They model bed capacity as isolation capacity and kept the number of available beds constant. Further, several studies of influenza look at the influence of anti-viral medication and vaccination programs.²¹⁻²⁵

In this paper, we present a model that incorporates EBOV propagation in an extended SEIR model. We incorporate endogenously modeled intervention capacities, and parameterize the model for Liberia. The parameterization happens in a Scenario Discovery approach where we sample over a broad bandwidth of input parameter values to account for the uncertainty characterizing the current EVD outbreak. This allows us to evaluate the influence of dynamic limits of EVD interventions on the effective reproductive number. As such, the effective reproduction number is modeled as the result of a SEIR model extended with endogenous intervention capacities. This theoretical paper thus tries to explain how the epidemic risk and the necessary intervention interact, what the consequences are of this interaction, and how the use of dynamic transmission models with integrated dynamic intervention capacities may inform planning of intervention capacities during future large outbreaks.

The setup of this paper is as follows. First, we explain how we developed the model, extending the SEIR model structure with limiting intervention capacities of isolation, health workers, tracing officers, and eventually vaccines, and the experimental setup. Second, we present the results of our analysis for the reproduction number, cumulative number of cases,

cumulative number of deaths, cases in isolation, and cases not in isolation. Third, we discuss our findings and potential future research directions, followed by the conclusions.

Methodology

We present a model combining a SEIR core with possible interventions aimed at stopping the Ebola epidemic in West Africa. The model is represented using System Dynamics (henceforth called SD).²⁶⁻²⁸ We use the model in a Scenario Discovery approach²⁹ to explore the consequences of the different combinations of uncertainties on the dynamics of the epidemic, and test the effects of different intervention strategies.

Model description

The SD model extends the traditional SEIR model by including a set of endogenous interventions. SD is a method for modeling and simulating dynamically complex systems or issues characterized by causal relations, feedback loops, accumulations, and delays. Although Causal Loop Diagrams and Stock-Flow Diagrams are used to explain the complexity of the system, which is characterized by feedback and accumulation effects, in an understandable way,³⁰ SD models are essentially systems of differential equations. Numerically integrating these equations results in a simulation of the dynamically complex behavior of the modeled system. This simulation can be used to analyze problems related to the system, and to evaluate the effects of policy interventions in these systems. SD is regularly used to study disease dynamics and health policy.^{27,31}

The central structure of the model contains a Susceptible, Exposed, Infectious, and Recovered population (Figure 1). We made several changes to this basic structure. We divided the infectious population in a critical phase, where patients may either recover or die. The recovering patients are still infectious. Therefore, they are modeled using a second stock variable, the infectious survived population, who are recovering and will survive. We subdivided (i.e., vectorized or subscripted) these population stocks to take into account that the population may start to apply some self-quarantining. We assume that infecting the self-quarantined population is more difficult than infecting the rest of the population, and that the self-quarantined infectious outside isolation are less infectious to their surroundings. The S, E, and I stocks outside isolation, and the flows between these stocks, thus contains this subdivision. In Figure 1, these stocks have a bold border. Introducing this structure is important, as a successful societal reaction to an outbreak leads to a significant decrease in necessary intervention capacities like isolation capacity. Next to this, motivating the population to change behavior in this way can be seen as an intervention itself.

Further, we added isolation capacity to the model, containing again two stocks for the critical and the survived infectious population. Treating and burying of the formally isolated happens at a lower infectivity rate, while the non-isolated deceased may still infect the susceptible population before their burial takes place. We, therefore, added a stock for the unburied deceased population. Finally, we included a stock for those who will be vaccinated when vaccines become available. This vaccinated population, and the recovered population, are assumed to be no longer susceptible to EBOV.

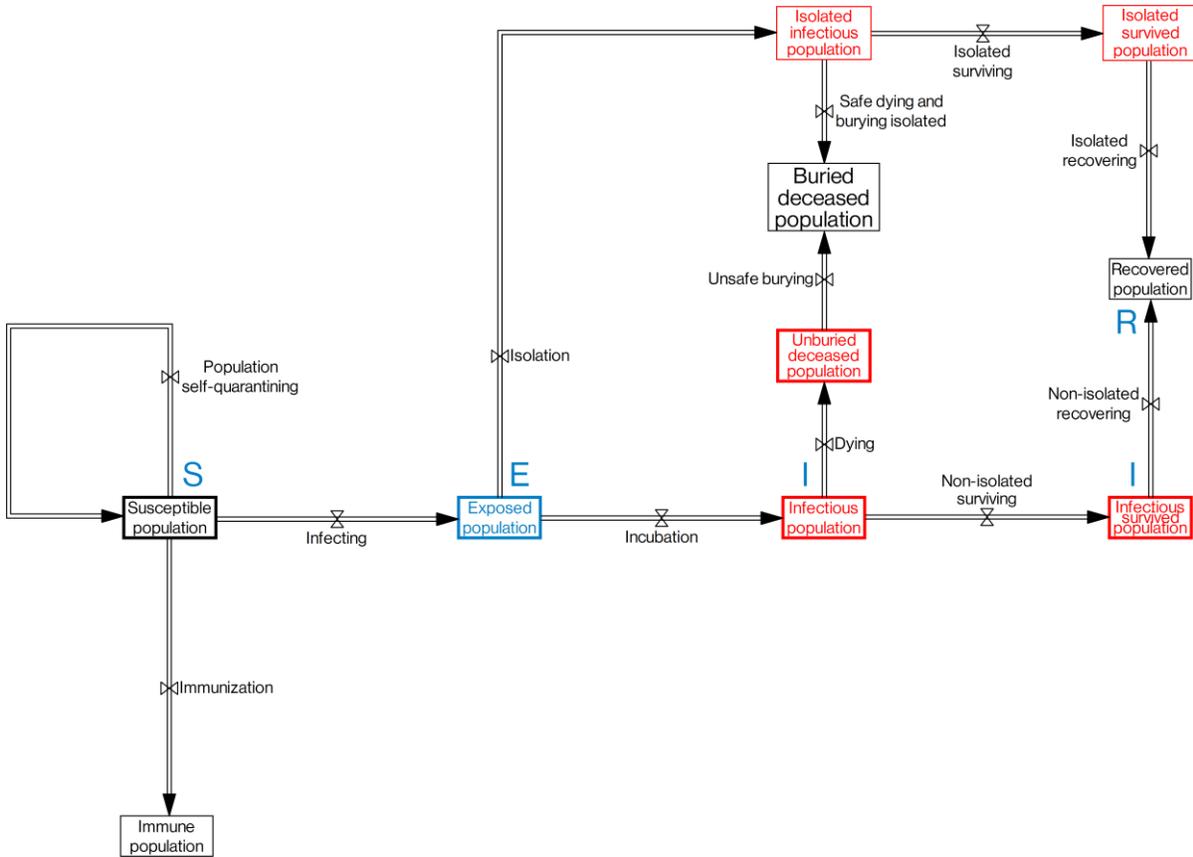


Figure 1. Stock-flow structure of the extended (other factors and causal relations are not shown) SEIR model containing isolated population stocks, and the immune population due to vaccination. SEIR elements are indicated with their respective letters as well. Subscripted stocks have a bold border, infectious stocks are red, and the exposed population is blue.

All interventions are limited in their capacity. Therefore, we included in this model the endogenous development of the availability of isolation capacity (i.e., beds), health workers, tracing officers, and vaccines. All intervention capacities are modeled as aging chains containing stocks for the preparation of capacity and the available capacity. These stocks are separated by delay time that may hinder timely reaction to an epidemic.^{32,33}

The capacities for isolation and other interventions are modeled adaptively: if needed, they are expanded, albeit delayed. In this way, the numbers of health workers, tracing officers, and available vaccines increase. For health workers, the possibility of getting infected by EBOV and consequentially dying of EVD is taken into consideration,³⁴ thus reducing their availability. We assume that fully recovered healthcare workers will try to continue their efforts after an extensive recovery time. Further, healthcare workers may be recruited domestically or from outside the region. All physicians needed are assumed to be foreign. Only a small portion of the susceptible population is considered suitable for nursing since they are not trained to protect themselves properly, but a larger part of the recovered population is suitable for nursing, since they are immune.

Finally, if the medical staff capacity is not sufficient for the isolation capacity, the isolation capacity will be limited following the available staff numbers. This represents the closing down of EVD treatment centers due to illness of staff.

Experimental setup

The model was implemented in the Vensim modeling software³⁵ and parameterized for the Liberian situation. The model contains 161 variables, of which 20 were subdivided for hygienic and normal behaving population (i.e., vectorized or subscripted), and 35 were considered uncertain. We simulated the model for 400 days, with a time step of 0.25 days using the Runge-Kutta 4 auto numerical integration method. For the 35 uncertain parameters, we used a Latin Hypercube sampling approach, based on the ranges in Table 1. We generated 10.000 samples. The model and scripts for the analysis can be found in the supplementary material.

Table 1. Uncertainties used as model input. Factors for which no literature reference exists, are indicated as assumption.

Variable name	Unit	Min	Max	References
Average contact rate infectious population	1/Day	0.3	0.9	3, 17, 37
Average development time isolation facilities	Day	4.2	18.8	Derived from reports like 36
Average infectivity for medical staff	1/Day	0.0087	0.046	Derived from analysis; 36
Average extra recovery time survivors	Day	0.5	4.66	3; Derived from analysis
Average time staff active	Day	185	341	Derived from analysis
Average time until burial	Day	0.5	2	37
Average time until return diseased health workers	Day	21	60	Assumption
Average period critical condition	Day	4	9	3
Case fatality rate in isolation relative to outside isolation	Dimensionless	0.43	0.73	Broad bandwidth around data from 3; Derived from analysis
Case fatality rate outside isolation	Dimensionless	0.45	0.86	3;
Contact rate before funeral	1/Day	0.32	0.97	Derived from 3,36;
Contacts to be traced per quarantined patient	Contact/Person	5.47	40	Bachinsky and Nizolenko (20)
Contacts traceable per tracer per day	Contact/(Person*Day)	10	40	Bachinsky and Nizolenko (20)
Delay time development new vaccines	Day	250	350	Assuming that vaccines will be available in first or second quarter of 2015
Doctors per nurse	Dimensionless	0.12	0.46	Assumption; Derived from analysis
Effect of self-quarantining behavior	Dimensionless	2.28	20	Assumption
Fraction recovered population useful as medical staff	Dimensionless	0.000458	0.043	Assumption; Derived from analysis
Fraction susceptible population useful as medical staff	Dimensionless	1.86E-06	0.000189	Assumption; Derived from analysis
Incubation period	Day	7	15	WHO Ebola Response Team ³
Initial exposed population	Person	50	100	WHO ³⁷
Initial isolation capacity	Person	120	600	WHO ³⁷
Initial relative susceptible hygienic population	Dimensionless	0.01	0.2	Assumption
Initial tracing personnel	Person	5	30	Assumption
Initial vaccines in preparation	Vaccine	4	20	Assumption
Lifetime isolation capacity	Day	180	360	Assumption; Derived from analysis
Medical staff creating awareness	1/Day	5	100	Assumption
Medical staff per new case	1/Day	0.2	0.5	WHO ³⁷
Preparing time foreign staff	Day	14	60	Assumption; Derived from analysis
Recognition rate diseased	Dimensionless	0.2	0.95	Broad bandwidth around WHO ³⁷
Relative reduction in infectivity due to isolation	Dimensionless	0.7	5	Assumption
Training time new staff	Day	3	10	Assumption
Vaccination speed	Vaccine/(Person*Day)	50	240	Assumption (estimate)

Results

Scenario selection

The epidemiological data provided by the WHO presents the number of cases and deaths measured to date. However, it is plausible that this data considerably underreports the actual number of EVD cases.¹⁹ The WHO acknowledges this in its roadmaps.³⁷ Therefore, we used both the *measured cumulative cases* and the *actual cumulative cases* as indicators for selecting the plausible scenarios from the total set of runs. The measured cumulative cases are the cases reported and found by tracing officers and the cases that report themselves. The actual cumulative cases are all cumulative EBOV infected cases. The measured cumulative cases was required to be minimally the reported number of cases, while the actual number of cases was required to be maximally 4 times the reported cases. Therefore, we take a slightly broader bandwidth than the potential underreporting correction factor of 2.5.¹⁹ Following this recipe, we were able to select 16 scenarios out of a total of 10000 model simulation runs.

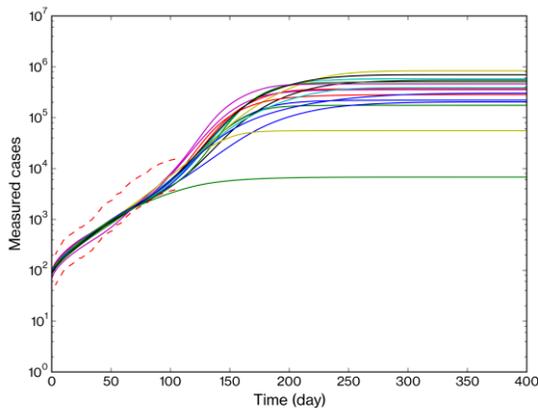


Figure 2. Dynamics for measured cases, historic data from WHO is indicated in dashed lines. The figure has a logarithmic y axis.

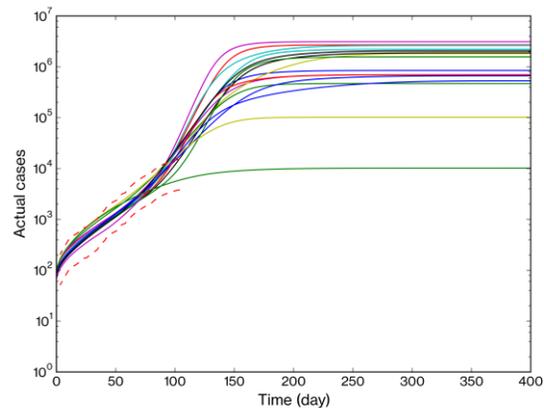


Figure 3. Dynamics for actual cases, historic data from WHO is indicated with dashed lines. The figure has a logarithmic y axis.

The 16 scenarios visible in Figure 2 and Figure 3 each provide a different internally consistent explanation of the measured data by the WHO. The runs start at the moment when the WHO reported 51 cases in Liberia, so $t=0$ can be interpreted as 22 June 2014. In the best-case scenario, the underreporting of cases is limited due to relatively sufficient tracing officers capacities. Consequentially, the required additional capacities for isolation and medical staff, as well as for the additional tracing officers, can be estimated adequately, resulting in a situation where the disease can be controlled before the whole population becomes infected.

In the worst-case scenarios, the tracing capacity is inadequate, which leads to inadequate development of isolation and medical staff capacity. This can be seen by comparing Figure 4 and

Figure 5. Figure 4 shows the total non-isolated infectious population, while Figure 5 shows the isolated infectious population. First, the peak in the non-isolated population is considerably earlier than the peak in the isolated population. In these instances, the intervention capacity has missed the real peak in the epidemic. Second, missing this peak makes that an order of magnitude difference exists between the maximum non-isolated infectious and the maximum isolated infectious in the worst-case scenarios.

In the worst-case scenarios, changes in population behavior (e.g., when part of the diseased actively seek help at treatment centers, even when they were not traced) will have less effect, as the required isolation capacity and treatment is not available. Therefore, it is the weakest link in the intervention capacities that determines the strength of the intervention capability.

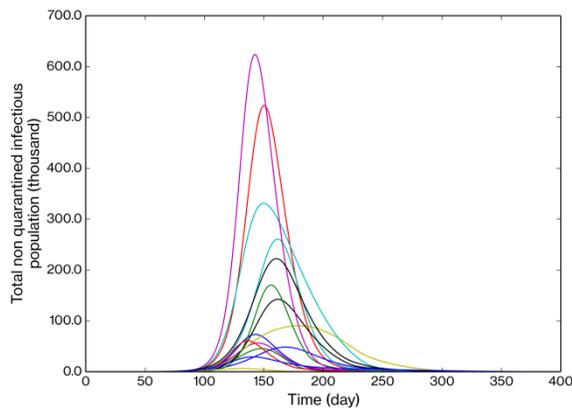


Figure 4. Total non-isolated infectious population dynamics

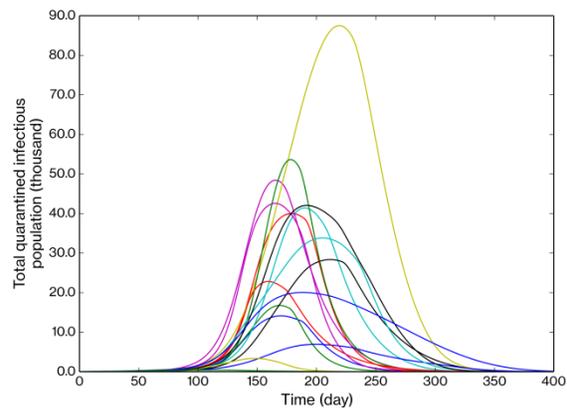


Figure 5. Total isolated infectious population dynamics

Limits in EBOV intervention capability influences the speed with which the virus is transmitted. The assumption underlying these dynamics is solely that an isolated EVD case is less infectious than a non-isolated EVD case. The results of this are illustrated in Figure 6, which shows how the reproduction number develops in the 16 scenarios. In the best-case scenario, the reproduction number will gradually decline as intervention becomes more effective. In the worst-case scenarios, however, we see that a failure to isolate a majority of EVD cases leads to a considerable increase in the reproduction rate of the disease, causing a significant increase in the effective reproduction number. As a result, we see that the doubling time of the number of cases declines (Figure 7). This indicates an increased spreading of EBOV, which leads to the break in current trends visible in Figure 2 and Figure 3. When the EBOV transmission is over its peak, the doubling time will quickly rise as the effective reproduction number falls below 1.0.

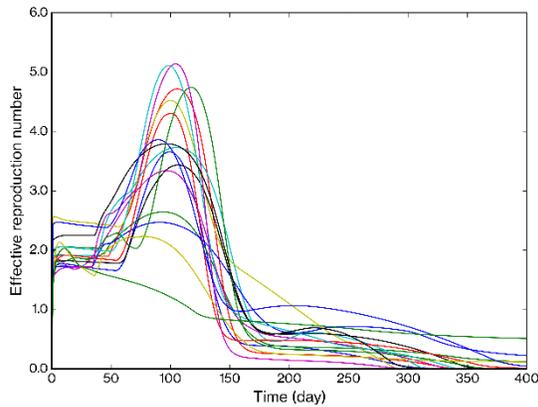


Figure 6. Effective reproduction number dynamics

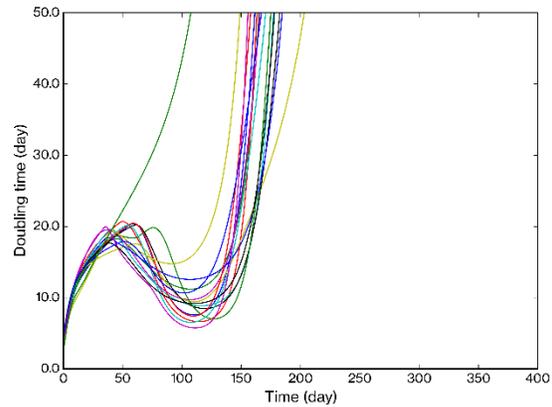


Figure 7. Doubling time dynamics

For two distinct reasons, scenarios showing an increased effective reproduction number may be plausible in the case of the 2014 West Africa EBOV epidemic. First, the reproductive number is the result of infectious people having contact with their surroundings (e.g., as they are being treated by family members, or in the case of unsafe burials). Therefore, if the relative share of infectious population that cannot be isolated increases, due to limitations in either available beds or available trained and well-equipped staff, then the effective reproduction number is also expected to increase. Second, many studies estimating the base reproductive number of EBOV or similar diseases assume that the intervention capability is not available at the beginning of the epidemic, while its adequacy increases over time (e.g., ^{13,38}). In the case of the 2014 EBOV epidemic in West Africa, however, it seems as though the intervention capability is getting less adequate over time (compare data in ³⁷), potentially resulting in the dynamics simulated here.

Effect of a more proactive approach

The response to the EBOV epidemic was initially inadequate, leading to a situation in which the outbreak could become out of control. The exponential character of the spreading of EBOV in the early phases of the outbreak might explain this. Since the response leading to an increase of the intervention capability is delayed, the capacities that become available will often fall short of the capacity required, especially when, for example, insufficient tracing capacities further increase the underreporting of the speed with which the virus propagates through society. Therefore, it may be needed to use a more proactive approach in increasing the intervention capacities, trying to be ahead of future increases in cases, while taking irreducible delays in the development of new capacities, into account. The following formula captures this kind of proactive planning:

$$C_{t+1} = c_u * C_{t,des} * \left(1 + \left(\frac{\tau_C}{\tau_2} \right) \right) - C_t$$

Where:

C_{t+1} is the capacity to develop;

c_u is the expected underestimation factor of the number of EVD cases;

$C_{t,des}$ is the presently desired capacity;

τ_C is the delay on capacity development;

τ_2 is the doubling time for the number of EVD cases;

C_t is current available capacity.

The motivation for this formula is that while preparing new intervention capacities, one should be prepared for those EVD cases that will arise during the preparation time, as well as the exposed population that will become infectious after the deployment of the additional capacities. If the preparation time is relatively short compared to the doubling time, the necessary extra capacity is, therefore, smaller. Existing capacity may be subtracted from the capacity to develop. It should be noted, however, that in the case of probable underreporting of the number of EVD cases, the presently desired capacity should be multiplied with the expected underestimation factor.

In any scenario, a more proactive approach will lead to a decrease in both the total number of cases (Figure 8) and the total number of deaths. However, the effectiveness of this change in intervention capacity development depends largely on the phase of the epidemic; when the spread of the virus is already decreasing and the doubling time is increasing (Figure 9), the potential gains are smaller.

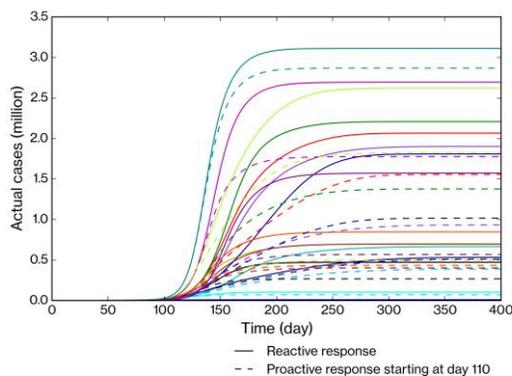


Figure 8. Total cases with proactive intervention expansion from day 110

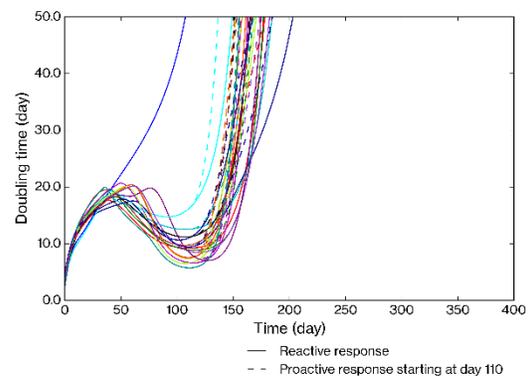


Figure 9. Doubling time dynamics with proactive intervention from day 110

The effectiveness of a more proactive approach is especially clear when it is applied earlier in the exponential growth phase of the epidemic (Figure 10 and Figure 11). These figures show the result of starting the proactive approach at day 50. The worst case is now logically the

scenario in which an initial underestimation of the size of the epidemic leads to an early increase in the reproductive number of the virus. Consequentially, it becomes more difficult to control the EBOV outbreak. An early proactive approach in building up the total spectrum of intervention capacities thus decreases the final scale of the epidemic, characterized by the cumulative cases, considerably.

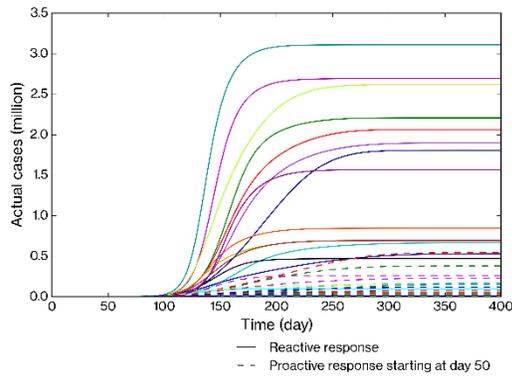


Figure 10. Total cases with proactive intervention expansion from day 110

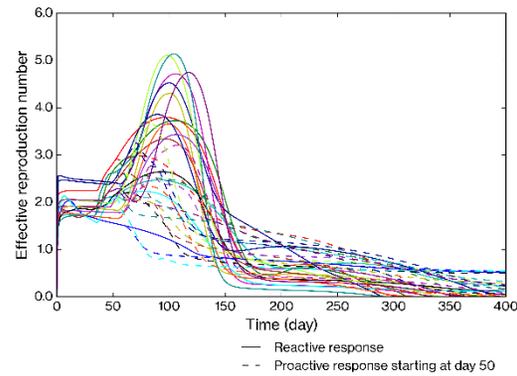


Figure 11. Total deceased with proactive intervention from day 110

Discussion

The results presented in this study provide plausible scenarios for the spread of the EBOV in Liberia, but should not be interpreted as forecasts of the future number of cases or deaths. Rather, we present an extended what-if analysis to explain how the epidemic might evolve under circumstances similar to the situation in Liberia in between June and October 2014.

For several reasons, the actual disease spread may be less dramatic than the worst-case scenarios presented in this study suggest. First, the geographic spread of the population may lead to a slower virus transmission. Within certain areas, the susceptible population may be, therefore, actually smaller than the assumption underlying our simulation model that the susceptible and infectious populations outside isolation are perfectly mixed. Further, this model does not contain possible social and psychological dynamics of the population that may considerably slow down EBOV transmission, nor the existence of asymptomatic infections and acquired immunity.³⁹

Finally, this research is not exhaustive in the possible intervention measures. We have not modeled essential medical supplies besides the medical staff and bed capacity in isolation. Further, we have assumed that the intervention capacities developed will not be hindered by lack

of available resource, for example skilled medical personnel, in foreign countries. However, the same principle applies to these other measures: Any under capacity will harm the effectiveness of the total intervention capability. The entire intervention capability is as strong as the weakest capacity in the chain.

Conclusions

In this article, we have demonstrated that the current under capacity in intervention measures for combatting the 2014 West Africa EBOV epidemic may lead to an increased effective reproduction number. The consequence of such a situation may be that the growth in the actual number of EVD cases accelerates significantly. This finding is derived from an extended SEIR model that includes key intervention capacities endogenously, parameterized for the situation in Liberia.

This research suggests that the reproduction number of the current Ebola epidemic may increase compared to the measured base reproduction number³ if the capacities of the different interventions are not brought to the minimally required level. Such a situation with sufficient intervention capacities is in contrast with the situation in the first half of October 2014 in Liberia, which shows a significant shortfall in bed capacity, caused by both a lack of health care staff and a lack of operational bed capacity in Ebola treatment units.⁴⁰

This under capacity may be caused by an overly reactive response to the initial exponential growth of the number of EVD cases. A more proactive approach in expansion of the intervention capacities may, therefore, help in controlling the 2014 West Africa EBOV epidemic, as well as future epidemics. A proactive approach takes into account how the development time of these capacities relates to the doubling time of the disease, and the factor by which the measured cases may be underreported. A proactive and faster reaction is especially important before the EBOV becomes endemic in the West African region.⁴¹

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