Modeling the Risk of the 2014 Ebola Epidemic

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The Ebola virus disease outbreak in West Africa has the potential to be one of the most deadly infectious disease events in a century. In spite of this, little has been published that projects the path that the outbreak is on in each country, and less has been produced that estimates the uncertainty in the impact of the epidemic. Here, we present a set of calculations estimating the range of possible trajectories the epidemic could take in Sierra Leone, Liberia and Guinea. We also provide a framework by which RMS will project and assess the progress the world has made in its mission to stop the epidemic over the coming months.

A month from now, it is likely that there will be 1000 new cases per day, and perhaps as many as 1400. Given that there have been over 9000 cases reported in total so far, this outbreak will get worse before it gets better.

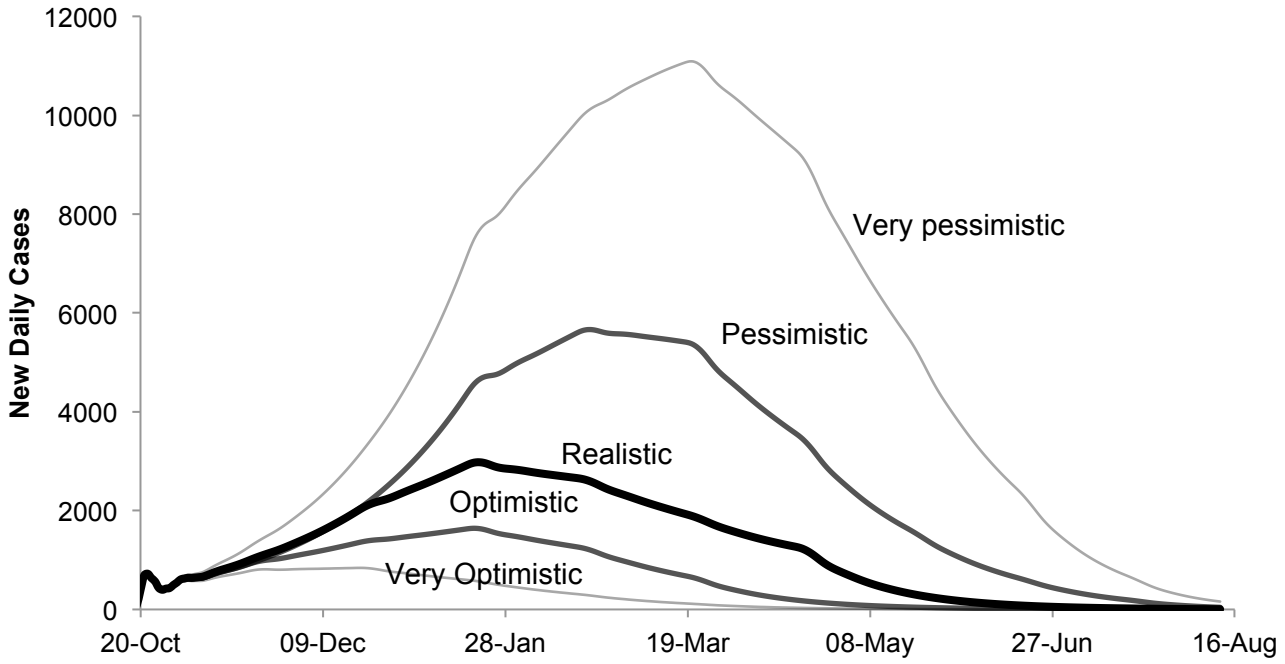

Figure 1: The Tipping Point

The number of days to reach the tipping point is critical. The five scenarios represent RMS's projections for the outbreak. Each is related to the pace at which control measures are put in place to slow down the rise in new daily cases. For each successive scenario, it takes an additional month to reach the tipping point and results in approximately double the total cases. Thus, the pace with which effective control measures are implemented is going to be the largest factor in determining the impact of this epidemic.

Modeling Ebola

Controlling the spread of this Ebola outbreak is more a question of logistics than one of virology. Treatments might help reduce the case fatality rate, but are very unlikely to have a significant role in halting the spread of the Ebola epidemic. An Ebola vaccine might be available in time to shorten the epidemic end game with doses available perhaps as soon as the New Year, but it will not be produced in sufficient quantities to have an active role in halting the spread of the epidemic in the next few months.

We have seen in Nigeria and in some sub-regions of the impacted countries that a coordinated response with effective case control and contact tracing can cut transmission to a level where the outbreak simply peters out. However, this gets harder as the number of current cases rises because the resources required in terms of hospital beds, healthcare workers, medical equipment, funding and on-the-ground coordination are roughly proportional to the number of cases. The U.S. Centers for Disease Control and Prevention (CDC) estimate that, even in the absence of treatments and vaccines, the epidemic would be brought under control and eventually come to an end if approximately 70-75% of cases are in medical care or treatment units or in environments where there is a reduced risk of disease transmission. The latter category includes safe burial, because Ebola can be caught from corpses.

Framed in this way, the epidemic becomes a race against a moving target. The ideal situation is that effective resources are deployed at a rate of increase that outstrips the pace of increase in new cases as early as possible. In this scenario, we reach a "tipping point" where the number of new daily cases reaches a maximum. Once this has happened, the response measures in place will be able to trace new contacts and prevent new infections at a rate that causes the epidemic to peter out – like a larger-scale version of Nigeria's successful control of its outbreak. Figure 1 shows how the tipping point could be reached under different scenarios of the world's effectiveness in responding to the epidemic.

Some very recent information suggests that the epidemic is back on the rise in Guinea after a period of slower increase in caseloads, and is exhibiting exponential growth in Sierra Leone. However, the recently very high rate of increase in Liberia may be slowing down. The typical method of measuring caseloads is to count the cases by week in which they were reported. Using this technique, it appears that cases are growing exponentially in Liberia. However, alternative reporting involves measuring the cases based on the week in which onset of symptoms took place. According to the WHO Ebola Response Team, very recent data reported in this way appears to show new cases in Liberia slowing down. If this slowdown is taking place, it is likely to be geographically patchy, with some districts achieving success and others struggling to halt spreading. RMS will continue to monitor these sources as more data becomes available.

Ebola Risk Management

RMS devised this set of forward-looking international response scenarios to model the future of the epidemic. The evolution of the Ebola epidemic can be simulated by modeling the progress of risk mitigation measures over the coming months. Because of the large potential variability in the timing, extent and effectiveness of the deployment and implementation of such measures, a risk perspective is insightful for future Ebola risk management.

We used (i) the current response resources in place in the impacted countries, (ii) further resources already pledged and (iii) a range of estimates of potential additional resources that will be deployed. For each country, we used these factors together to formulate the five scenarios and their associated probabilities, those scenarios ranging from very optimistic to very pessimistic. Figure 2 displays the number of beds currently in use for effective isolation and treatment, together with the peak number of beds in use required to turn the epidemic around in each of our scenarios. The number of beds for Ebola treatment currently in use is far below what is needed to reverse the outbreak in any of the three countries. To reach the tipping point sooner, fewer total beds and resources in general are required, but faster ramp up is essential. For example, in order to reach the

tipping point in Sierra Leone, the current number of beds in use needs to be approximately tripled by the end of November to halt the outbreak with the smallest total number of cases and at the lowest overall cost. If that fails, the number will need to increase to six times today's number by the end of December to halt the outbreak.

A large degree of reliance will be placed on beds being rolled out in Ebola treatment centers (ETCs), the gold standard specialized clinical environments for treating patients and preventing further transmission. This is no easy task, with $5.7 million the cost to set up and run a fifty-bed center for one month. There is also some effort going into setting up Ebola community care units (ECUs) staffed by rapidly trained non-experts rather than medical workers. Some efficacy of ECUs has been assumed in our calculations, but the larger uncertainty in the possible impact of these measures has also been taken into account.

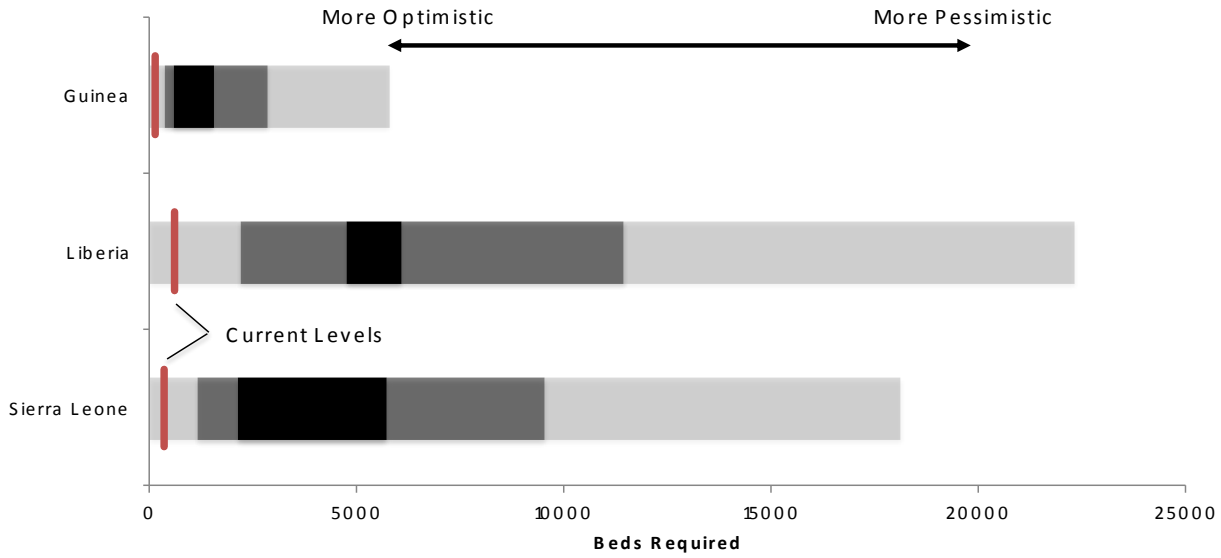

Figure 2: Beds Required Per Day By Scenario

This shows the number of beds with effective isolation required per day for each scenario to reach its tipping point. The lightest grey cases represent the *very optimistic* and *very pessimistic* cases (the left-most and right-most bars respectively), the mid-grey the *optimistic* and *pessimistic* cases, and black the *realistic* cases. A month slower means moving a whole scenario to the right (with the corresponding increase in the number of beds needed), whereas a month faster means moving a whole scenario to the left and cutting the total number of beds needed [1], [2], [3].

We projected the number of cases in each of these scenarios using the CDC's susceptible-infected-recovered model of the outbreak, the same class of model used in the RMS Infectious Disease Model [4]. As the numbers of beds in ETCs and ECUs change over time, and as new caseload data becomes available, RMS will revise its estimates taking account of the new data.

This virus is extremely deadly, with an estimated case fatality rate of 69-73% [5]. Current estimates suggest that cases in children and the old are slightly more likely to be fatal than in 15-44 year olds. Altogether, the age mortality distribution appears to be relatively flat, consistent with the extreme pathological response of the virus. Hospitalization is also credited with reducing the case fatality rate from around 70% to 64%. While medical treatment may reduce the odds of fatality, part of this lower rate of death is caused by the fact that it takes an average of five days for a suspected case to be hospitalized. Therefore, rapidly deteriorating cases can be excluded from the hospitalized figures because those people die before they are admitted.

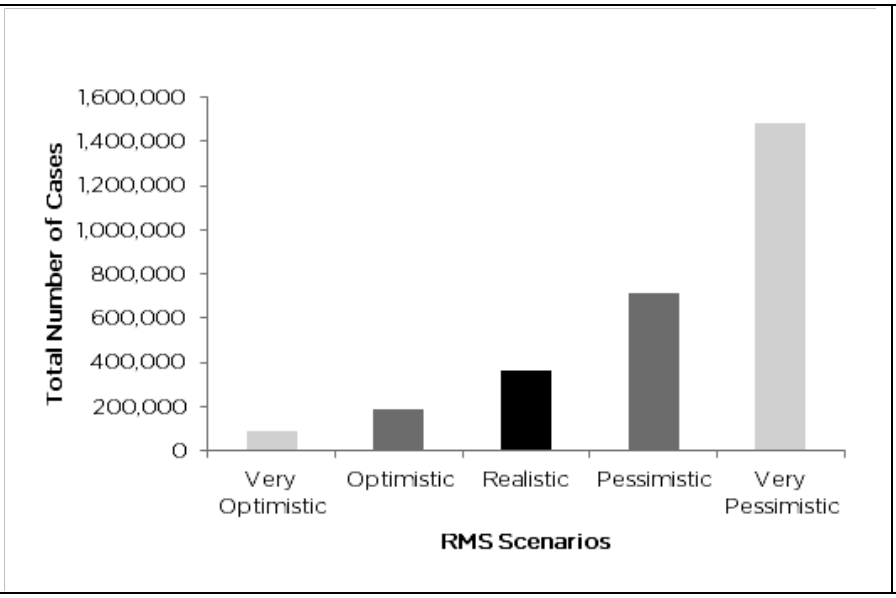

Figure 3: RMS Scenarios - Number of Cases

The total numbers of cases were projected using the separate country models from the CDC and RMS's projections of the interventions. For every month's delay in reaching the tipping point, the number of cases effectively doubles.

Ebola in the Rest of the World

RMS does not expect this outbreak of Ebola to become a significant mortality threat in other parts of the world. It is possible that it could spread to neighboring countries in West Africa, although this risk can be reduced by appropriate screening of people leaving the impacted region and could be contained with rapid implementation of effective control measures.

In the situation where there are potentially 10,000 new cases per week in West Africa, there will be more cases imported into other countries. This is possible via two routes. Foreign workers combating the spread of the virus are likely to be repatriated to their home countries. Currently the United States, United Kingdom, France and Cuba are the countries that have delivered personnel in significant numbers. RMS does not consider this to be a probable source of escalating cases in those countries (or in others with the ability to join the effort), since such cases will be monitored and appropriately isolated by the stronger public health systems already in place in those countries. The second such route is via infected people travelling to other regions unchecked. While such a scenario is possible, the capability of most countries to trace contacts is far higher than in Liberia and Sierra Leone, and stronger travel control measures could be implemented if case numbers exceeded a prudent limit.

Medical Interventions

Treatments

There are five experimental drugs currently being investigated as Ebola virus treatments. ZMapp, a monoclonal antibody drug, is the most well known of these, and has proven efficacious in a trial with macaques. Of the five courses of treatment administered to humans, three have survived and two have died. Currently the manufacturer's inventory of this drug is very low and it will struggle to make more to have a significant impact on this epidemic. Another promising drug targets the ability of the virus to reproduce its RNA in the host's cell. It has also looked good in primate trials but has not been tested on humans yet. Three further candidate drugs are also promising, but are in similarly early stages of testing and production.

Transfusion of survivors' blood serum to the infected is another potential form of treatment. Particles left over from the infection of the survivor may be able to neutralize the virus. While this has potential to be an effective treatment, it is difficult to

administer unless there are sufficient Ebola treatment centers (ETCs) to both extract the serum and administer it to patients safely.

Vaccines

There are three vaccines currently under investigation. Several of them have shown promising performance in pre-clinical trials on primates, and are now being tested for efficacy and safety on humans. It is unlikely that these trials will be complete soon, with optimistic estimates suggesting that 20,000 doses could be available for at least one of the vaccines in the New Year. This leaves a lot of time for the number of cases to rapidly increase; however, if a vaccine is effective and administered efficiently, it could have a significant impact on reducing cases in early 2015.

Ebola Epidemic FAQs

How is it possible to cut infections by non-pharmaceutical interventions alone?

This is largely owing to the mechanism by which the virus spreads. Transmission is via direct contact with the bodily fluids of a person showing symptoms or the recently deceased; indeed, the likelihood of being infected increases as the symptoms worsen and is at its highest around the time of death. With no transmission by aerosol or a period of infectiousness where no symptoms present, it is much easier to identify potential infections (known as "contacts"). They can be traced, isolated and treated if necessary.

How did Nigeria halt the outbreak?

Nigeria's index case was Liberian diplomat Patrick Sawyer. He was already identified as ill before departing on a flight from Monrovia to Lagos. He collapsed after arrival at Lagos airport and was transported to hospital, where he later died. The Nigerian authorities traced all of Sawyer's contacts, and one doctor in particular prevented Sawyer from leaving the hospital. This act is credited with potentially saving many lives. This action contained the outbreak in Nigeria to nineteen cases and eight deaths, many of who were healthcare workers who treated Sawyer in hospital. The WHO officially now labels Nigeria an Ebola-free country as six weeks have passed since its last case.

What is R_0?

The basic reproductive number R_0 is the average number of people an infected person will infect in a susceptible population. Assuming no intervention, when $R_0 > 1$, the outbreak will continue exponentially; conversely, with $R_0 < 1$, the epidemic will peter out. This outbreak of Ebola has an R_0 of 1.5 to 2.2 [5]. The breadth of this range is due in part to different estimates of R_0 in each country. Another important parameter is R_t, the equivalent parameter to R_0 but viewed over time and with the impact of interventions. The lower R_t, is, the better interventions are working and the more likely the epidemic will be stopped.

How deadly is Ebola?

The case fatality rate for the Ebola epidemic is estimated at 69%-73% based on recorded definitive clinical outcomes [5]. Since these do not represent unreported cases, further uncertainty exists in these numbers. Treatments may be able to reduce the lethality, but the main candidates are as yet unproven.

What is happening to treatment of other diseases in the impacted countries?

The medical systems are overwhelmed by the Ebola outbreak in all three countries, so there has been greater mortality experience from other diseases (malaria, yellow fever) than usual. As malaria season reaches its peak, this is likely to worsen.

The RMS LifeRisks Infectious Disease Model includes scenarios for many combinations of virulence and transmissibility, along with the impacts of medical interventions, non-medical interventions, vaccines, and population characteristics to project potential impacts of influenza or emerging infectious disease pandemics on insured populations. This includes scenarios for how diseases like Ebola, MERS, H1N1, or a newly emerging disease could act as pandemics.

References

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