A Model of the 2014 Ebola Epidemic in West Africa with Contact Tracing

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Abstract

A differential equations model is developed for the 2014 Ebola epidemics in Sierra Leone and Liberia. The model describes the dynamic interactions of the susceptible and infected populations of these countries. The model incorporates the principle features of contact tracing, namely, the number of contacts per identified infectious case, the likelihood that a traced contact is infectious, and the efficiency of the contact tracing process.The model is first fitted to current cumulative reported case data in each country. The data fitted simulations are then projected forward in time, with varying parameter regimes corresponding to contact tracing efficiencies. These projections quantify the importance of the identification, isolation, and contact tracing processes for containment of the epidemics.

1 Introduction

A variety of mathematical models of the 2014 Ebola outbreaks in West Africa have been developed ([1], [3], [4], [5], [6], [9], [13], [14], [15], [16], [17], [19], [28]). Our objective is to develop a mathematical model of the 2014 Ebola epidemic in West Africa incorporating contact transmission. The model consists of a system of ordinary differential equations for the compartments of the epidemic population. The model incorporates the unique features of the Ebola outbreaks in this region. These features include the rates of transmission to susceptibles from both infectious cases and improperly handled deceased cases, the rates of reporting and isolating these cases, and the rates of recovery and mortality for these cases. The model also incorporates contact tracing of reported infectious cases, and analyzes the efficiency of the identification and isolation of these cases, and the efficiency of contact tracing measures.

We apply the model to Sierra Leone and Liberia, first fitting WHO data for each country from outbreak in the spring of 2014 to September 23, 2014. We view this last date as a hypothetical starting date for the beginning of organized efforts to control the epidemics in these countries. We then simulate forward projections of the epidemic in each country, based on varied efficiencies in identifying, isolating, and contact tracing of infected individuals. Our model predictions indicate that the containment of the epidemic requires a high level of both the general identification and isolation process and the contact tracing process for removing infectious individuals from the susceptible population.

2 The Model

The model, which is of SEIR form ([1],[3],[11],[12]), incorporates specific features of contact tracing in the current epidemics. The model consists of the populations at time t of susceptibles $S(t)$ (capable of becoming

infected), exposed $E(t)$ (incubating infected), $I(t)$ (infectious infected), contaminated deceased $C(t)$ (improperly handled corpses of infected), isolated infectious $II(t)$ (exposed and infectious infected who have been identified and isolated from the susceptible population), and removed $R(t)$ (infected cases who have recovered or died). The compartments $II(t)$ and $R(t)$ de-couple from the other compartments, and their values can be obtained from $S(t)$, $E(t)$, $I(t)$, $C(t)$. A schematic diagram of the model is shown in figure 1. The system of differential equations for $S(t)$, $E(t)$, $I(t)$, $C(t)$ is

$$\begin{aligned}
\dot{S}(t) &= -\beta S(t)\frac{I(t)}{N} - \epsilon S(t)\frac{C(t)}{N} \\
\dot{E}(t) &= \beta S(t)\frac{I(t)}{N} + \epsilon S(t)\frac{C(t)}{N} - \sigma E(t) \\
\dot{I}(t) &= \sigma E(t) - \alpha I(t) - \gamma I(t) - \nu I(t) - \kappa(\alpha I(t) + \psi C(t))\pi\omega \\
\dot{C}(t) &= \nu I(t) - \psi C(t)
\end{aligned} \tag{1}$$

We note that the transmission terms in the $\dot{S}(t)$ equation are of mass-action form.. We assume that the initial conditions and parameters are specified so that $I(t)$ remains nonnegative for all time in a realistic time frame. The parameters of the model are given in Table 1.

A major goal of our study is to fit the model to current reported data for Sierra Leone and Liberia. We note that the data available are the cumulative clinical reported cases [23, 24], that is, the suspected cases, probable cases and confirmed cases according to the definitions given in WHO [25]. We also add to the reported cases the identified deceased when they are properly handled. The rate of transition from onset of symptoms to hospitalizatio is α. The rate of transition from improperly handled to properly handled is ψ. Therefore, if we denote by $CUM(t)$ the cumulative reported cases at time t, then at time $t + \Delta t$ we have

$$CUM(t+\Delta t) = CUM(t) + \underbrace{\int_t^{t+\Delta t} \alpha I(s)\, ds}_{\substack{\text{number of identified/isolated} \\ \text{infectious individuals in} \\ \text{the time interval } (t,t+\Delta t)}} + \underbrace{\int_t^{t+\Delta t} \psi C(s)\, ds}_{\substack{\text{number of deceased identified} \\ \text{and properly handled in} \\ \text{the time interval } (t,t+\Delta t)}} \tag{2}$$

The cumulative fraction of unreported cases at time t is $CUM(t)/(N - S(t))$. In order to fit the data we will use the above equation (2) with $\Delta t = 1$ day and $CUM(0) =$ the initial cumulative reported cases. We note that to simplify the model, we have omitted the infection dynamics of hospital and healthcare workers. Although healthcare worker infections from patients is of great importance and requires major attention, the contribution of healthcare worker infections to new transmissions and to the cumulative reported cases (2) is relatively small. In our model the parameter α is the rate per day symptomatic cases are reported (hospitalized). The issue of unreported cases is very important for contact tracing and, in general, the number of unreported cases is unknown. An advantage of our model is that the number of unreported cases can be determined from the model output. A major goal of contact tracing is to remove from the epidemic population a sufficient number of infectious cases to contain the epidemic, but only reported cases are contact traced.

3 The Parameters of the Model

The values of the parameters β, ϵ, ψ and α are estimated for the two countries using a least square curve fitting algorithm. The parameters σ and ν are taken to be values suggested by references in Table 1. The parameter γ is assumed to be a value such that the case mortality rate (outside hospital) is approximately 80%. In fitting the model to the data, we assume that contact tracing does not occur ($\kappa = 0$) during the time period of the data (up until September 23, 2014). The reasons for this assumption are that contact tracing has been insufficient to contain the epidemic in the two countries, and also to reduce the number of parameters to estimate in fitting the data. The main goal for incorporating contact tracing is to project forward how effective contact tracing can impact the number of future cases.

The basic reproduction number of the model (1) is given by the following formula (computed by the next generation method [20]):

$$\mathcal{R}_0 = \frac{\beta}{(\alpha+\nu)(1+\kappa\pi\omega)+\gamma} + \frac{\nu\epsilon}{\psi((\alpha+\nu)(1+\kappa\pi\omega)+\gamma)}.$$

Parameter/Variable	Description
N	Total national population (assumed to be constant)
β	Transmission rate excluding improper handling of deceased [1],[13],[16]
ϵ	Transmission rate due to improper handling of deceased [13],[16]
κ	Average number of contacts traced per identified/isolated infectious individual
α	Rate of removal (hospitalization) of infectious individuals independent of contact tracing [1],[11],[13],[16]
π	Probability a contact traced infected individual is isolated without causing a new case
ω	Probability a contact traced individual is infected
γ	Rate of removal of infectious individuals due to recovery (independent of hospitalization) [1],[11],[13],[16]
ν	Rate of removal of infectious individuals due to recovery (independent of hospitalization) [1],[11],[13],[16]
$1/\sigma$	Average incubation period [1],[11],[13],[16]
ψ	Rate of removal (identification) of improperly handled deceased cases [1],[13],[16]

Table 1: Model parameters.

The $\mathcal{R}_0$ values we obtain are similar to the $\mathcal{R}_0$ values obtained in [1],[3],[5],[6], [19], [26]. The value of $\mathcal{R}_0$ is as an approximate measure of the influence of various parameters on the number of secondary cases caused by an infectious individual.

The removal rate of infectious individuals due to contact tracing at time t has the following form:

$$\underbrace{\alpha I(t) + \psi C(t)}_{\substack{\text{rate of reporting of}\\ \text{infectious or deceased}\\ \text{individuals at time t}}} \times \underbrace{\kappa}_{\substack{\text{average number of}\\ \text{contact traced individuals}\\ \text{per reported case}}} \times \underbrace{\pi}_{\substack{\text{probability a traced contact}\\ \text{individual is successfully}\\ \text{monitored and isolated}}} \times \underbrace{\omega}_{\substack{\text{probability contact traced}\\ \text{individual is infected}}}$$

The probabilities ω and π can, in principle, be ascertained from records of contact traced cases over an interval of time. We note that the probability ω that a traced contact is infected will depend on the average number of traced contacts κ. The values of ω, κ, and π can be updated as health authorities collect data of hospitalized and deceased cases. The parameter π measures the efficiency of the tracking, monitoring, and removal of contact traced infectious cases for a specific organization and implementation of a contact tracing process. In particular, π measures how efficiently public health workers remove infected individuals upon symptoms onset, and prevent secondary transmissions. The solution of the model projects the likelihood that an implemented contact tracing process will contain the epidemic, and if not, then the contact tracing process must be enhanced.

The entire contact tracing process is highly dependent on public health resources, and varies greatly in different locations and epidemic stages. For example, in Sénégal the following policy has been implemented:

1) each identified patient is questioned in order to obtain a complete list of contacts;
2) the contacts are traced;
3) each contact is asked to stay at home;
4) each day, for 21 days, a healthcare worker visits the contacts and verifies whether or not the contacts are showing symptoms.

These protocols are rigorous and have been successful in preventing new cases in Sénégal. On October 17, 2014 the World Health Organization declared the end of the outbreak of the Ebola epidemic in Sénégal (after 42 days with no new cases and with active surveillance demonstrably in place and supported by good diagnostic capacity) [27] .

4 Simulations of the Ebola Epidemic in Sierra Leone

In Figure 2 we fit the model without contact tracing to the cumulative reported case data for Sierra Leone from May 27, 2014 to September 23, 2014 (WHO [23, 24]). The fit to data can be accomplished with varying combinations of parameters. Here we have used a least-squares algorithm to obtain a choice of parameters with relatively accurate fit. The parameters obtained in the fit yield a basic reproduction number of $\mathcal{R}_0 = 1.26$. The simulation yields the following information about the epidemic on September 23, 2014 (day 119): the ratio of exposed cases to infectious cases is $E(119)/I(119) \approx 2.49$; the ratio of improperly handled deceased cases to infectious cases is $C(119)/I(119) \approx 0.57$; and the ratio of cumulative reported cases to cumulative

unreported cases is ≈ 1.78. These ratios, which are dependent on parameters, are relatively stable at the data end-stage. In Figure 3 we graph the model simulation of the projected fraction of cumulative reported cases as a function of time without contact tracing. The fraction of cumulative reported cases to total cases shows a two phase behavior with a lower value transitioning to an upper value. In Figure 4 we add contact tracing to the model and predict the further evolution of the epidemic in Sierra Leone forward from September 23, 2014. The parameters α and κ are varied in a sensitivity analysis, while π is held constant. The graphs reveal that a general identification/isolation rate $\alpha > 0.3$ is required for containing the epidemic. The average number of contacts traced per reported case κ is also important if α is smaller. After contact tracing begins and for a short time, the reported cases increase as κ increases, but then the epidemic subsides as contact tracing takes effect.

5 Simulations of the Ebola Epidemic in Liberia

In Figure 5 we fit the model without contact tracing to the cumulative reported case data for Liberia from June 17, 2014 to September 23, 2014 (WHO [23, 24]). We have used a least-squares algorithm to obtain a choice of parameters with relatively good fit (other parameter choices will give similar fits). The parameters obtained in the fit yield a basic reproduction number of $\mathcal{R}_0 = 1.54$. The simulation yields the following information about the epidemic on September 23, 2014 (day 98): the ratio of exposed cases to infectious cases is $E(98)/I(98) \approx 3.35$; the ratio of improperly handled deceased cases to infectious cases is $C(98)/I(98) \approx 0.58$; and the ratio of cumulative reported cases to cumulative unreported cases is ≈ 1.37. These ratios, again dependent on parameters, are very stable throughout most of the period of simulation. In Figure 6 we add contact tracing to the model and predict the further evolution of the epidemic in Liberia forward from September 23, 2014. The parameters α and π are varied in a sensitivity analysis, while κ is held constant. The graphs again reveal that an identification/isolation rate $\alpha > 0.3$ is required for containing the epidemic. The role of π, as the probability of efficiently tracing and monitoring a contact traced individual is also important for the containment of the epidemic. As in Figure 3, the reported cases increase for a short time as π increases, but then decrease as contact tracing takes effect.

6 A Stochastic Version of the Model

Figure 7 shows 100 stochastic simulations compared with the ODE solution for contact tracing in Sierra Leone with different rates of case hospitalization α. The stochastic simulations are generated by simulating a continuous time Markov chain as a continuation of the ODE solution beginning at the last data time point. The parameters are t the same as in the Figure 4. The averages of the stochastic model solutions agree with the ODE solutions of (1).

7 Summary and Conclusions

We have developed a model of Ebola epidemics in West Africa that focuses attention on the elements of public health policies for containment of these epidemics. Our simulations for Sierra Leone and Liberia fit the cumulative reported cases for these countries up to September 23, 2014, and project future epidemic levels forward from September 23, 2014 (based on various parameterizations corresponding to these elements). Our projections indicate that the most important elements for containment of the epidemics within a relatively short time span are that

(1) infectious cases (independent of contact tracing) are efficiently reported and isolated, with the average time between the appearance of symptoms and isolation less than 3 days ($\alpha > 0.3$);

(2) contact traced infected cases are efficiently monitored, with average probability of compliance and isolation upon appearance of symptoms resulting in no new cases caused by the contacted individual greater than 50% ($\pi > 0.5$).

Also of importance in mitigation of the epidemics is a reduced rate at which infected deceased are improperly handled (ψ, ν), a sufficient number of contacts traced per identified infectious individual (κ). The model allows quantification of the parameters α, ψ, κ, π, ω corresponding to public health controls for evaluating the impact of public health policies for the evolution of these epidemics.

References

[1] C. L. Althaus, Estimating the reproduction number of Zaire ebolavirus (EBOV) during the 2014 outbreak in West Africa, *PLOS Currents Outbreak*, September 2, 2014.

[2] Center for disease control and Prevention, What is contact tracing? Contact tracing can stop the Ebola outbreak in its track. http://www.cdc.gov/vhf/ebola/pdf/contact-tracing.pdf

[3] G. Chowell, N.W. Hengartner, C. Castillo-Chavez P.W. Fenimore, J.M. Hyman, The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda. *J. Theoret. Biol.*, **229** (2004) 119-126.

[4] G. Chowell, L. Simonsen, C. Viboud, Y. Kuang, Is West Africa approaching a catastrophic phase or is the 2014 Ebola epidemic slowing down? Different models yield different answers for liberia, *PLOS Currents Outbreak*, November 20, 2014.

[5] D. Fisman, E. Khoo, A. Tuite, Early epidemic dynamics of the West African 2014 Ebola outbreak: Estimates derived with a simple two-parameter model. *PLOS Currents Outbreak*, September 8, 2014.

[6] M. Gomes, A. Pastore y Piontti, L. Rossi, D. Chao, I. Longini, M. Halloran, A. Vespignani, Assessing the international spreading risk associated with the 2014 West African Ebola outbreak. *PLOS Currents Outbreak*, September 2, 2014.

[7] Haas C.N.Haas, On the quarantine period for Ebola virus, *PLOS Currents Outbreak*, October 14, 2014.

[8] X. Huo, Modeling of contact tracing in epidemic populations structured by disease age. *to appear*.

[9] M. Kiskowski, A three-scale network model for the early growth dynamics of 2014 West Africa Ebola epidemic, *PLOS Currents Outbreak*, November 13, 2014.

[10] D. Klinkenberg, C. Fraser, H Heesterbeek, The effectiveness of contact tracing in emerging epidemics, *PLOS One*, **1** (2006) 1-7.

[11] J. Legrand, R.F Grais, P.Y. Boelle, A.J. Valleron, A. Flahault, Understanding the dynamics of Ebola epidemics. *Epidemiology and Infection*, **135 (4)** (2007) 610-621.

[12] P. Lekone and B. Finkenstädt, Statistical inference in a stochastic epidemic SEIR model with control intervention: Ebola as a case study. *Biometrics*, **62** (2006) 1170-1177.

[13] M. Meltzer, C. Atkins, S. Santibanez, B. Knust, B. Petersen, E. Ervin, S. Nichol, I. Damon, M. Washington, Estimating the future number of cases in the Ebola epidemic Liberia and Sierra Leone, 20142015. *CDC Centers for Disease Control and Prevention*, September 26, 2014, **63** 1-14.

[14] H. Nishiura and G. Chowell, Early transmission dynamics of Ebola virus disease (EVD), West Africa, March to August 2014. *Eurosurveil.*, **19 (36)** (2014), September 11, 2014.

[15] A. Pandey, K.E. Atkins, J. Medlock, N. Wenzel, J.P. Townsend, J.E. Childs, T.G. Nyenswah, M.L. Ndeffo-Mbah, A.P. Galvani, Strategies for containing Ebola in West Africa, published online in *Science*, October 30, 2014.

[16] C. Rivers, E. Lofgren, M. Marathe, S. Eubank, B. Lewis, Modeling the impact of interventions on an epidemic of Ebola in Sierra Leone and Liberia. *PLOS Currents Outbreak*, November 6, 2014. (revised).

[17] J. Shaman, W. Yang, S. Kandula, Inference and forecast of the current West African Ebola outbreak in Guinea, Sierra Leone and Liberia, *PLOS Currents Outbreak*, October 31, 2014.

[18] T. Stadler, D. Kühnert, D. A. Rasmussen, L. du Plessis, Insights into the early epidemic spread of Ebola in Sierra Leone provided by viral sequence data, *PLOS Currents Outbreak*, October 6, 2014.

[19] S. Towers, O. Patterson-Lomba, C. Castillo-Chavez, Temporal Variations in the Effective Reproduction Number of the 2014 West Africa Ebola Outbreak. PLOS Currents Outbreaks. 2014 Sep 18. Edition 1. doi: 10.1371/currents.outbreaks.9e4c4294ec8ce1adad283172b1

[20] P. van den Driessche and J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Math. Biosci.*, **180** (2002) 29-48.

[21] E. Volz, S. Pond, Phylodynamic analysis of Ebola virus in the 2014 Sierra Leone epidemic, *PLOS Currents Outbreak*, October 24, 2014.

[22] World Health Organization, Ebola Response Roadmap Situation Report 3, 12 September 2014. http://apps.who.int/iris/bitstream/10665/133073/1/roadmapsitrep3eng.pdf?ua=1

[23] World Health Organization, Ebola virus disease, *Global Alert and Response (GAR).* http://www.who.int/csr/don/archive/disease/ebola/en/

[24] World Health Organization, Situation reports: Ebola response roadmap, *Global Alert and Response (GAR).* http://www.who.int/csr/disease/ebola/situation-reports/en/

[25] World Health Organization, Case definition recommendations for Ebola or Marburg Virus Diseases. http://www.who.int/csr/resources/publications/ebola/ebola-case-definition-contact-en.pdf?ua=1

[26] World Health Organization, Ebola Response Team, Ebola virus disease in West Africa –The first 9 months of the epidemic and forward projections. *N. Engl. J. Med*, September 23, 2014.

[27] World Health Organization, Ebola situation assessment. http://www.who.int/mediacentre/news/ebola/17-october-2014/en/

[28] D. Yamin, S. Gertler; M.L. Ndeffo-Mbah, L.A. Skrip, M.a Fallah, T.G. Nyenswah, F. L. Altice, and A.P. Galvani, Effect of Ebola progression on transmission and control in Liberia, *Ann. Int. Med.*, **162** (2015) 11-17.

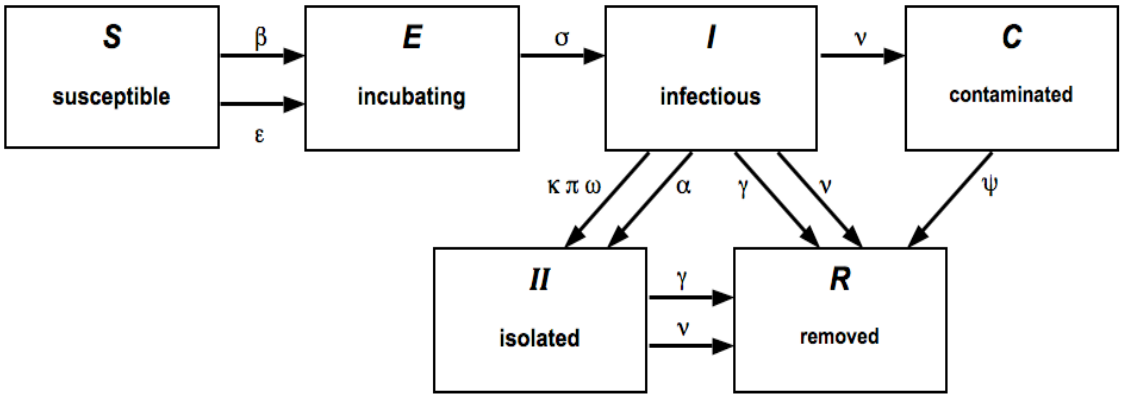

Figure 1: Schematic diagram of the model compartments and parameters.

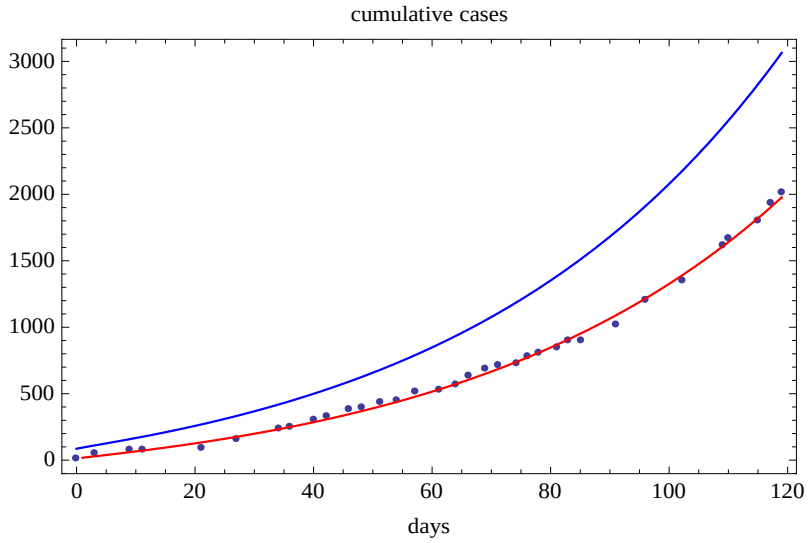

Figure 2: Simulation of cumulative cases in Sierra Leone from May 27, 2014 to September 23, 2014. The black dots are data of cumulative reported cases (WHO), the red graph is the model simulation of cumulative reported cases, and the blue graph is the model simulation of cumulative total cases. The parameter values are $N = 6,000,000$, $\beta = 0.32$, $\epsilon = 0.0078$, $\psi = 0.2$, $\alpha = 0.1$, the initial conditions are $S(0) = N$, $E(0) = 47$, $I(0) = 26$, $C(0) = 12$. $\mathcal{R}_0 = 1.26$.

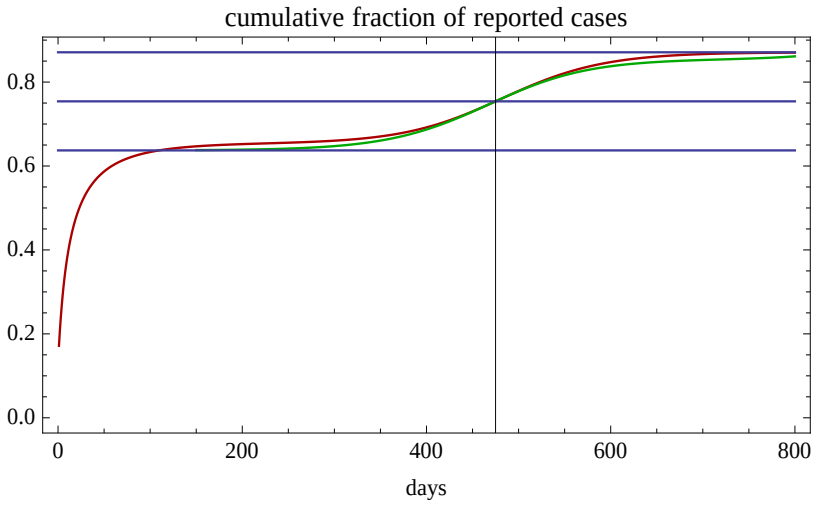

Figure 3: Simulation without contact tracing of the fraction of cumulative reported cases (red graph) in Sierra Leone from May 27, 2014 forward until day 800. The green graph is the reflected and mirrored image of the red graph about the time point 475 days, when $I(t)$ attains a maximum value. The top horizontal line is $(\alpha + \nu)/(\alpha + \nu + \gamma) \approx 0.871$ (the second plateaux). The middle horizontal line is the cumulative fraction of reported cases at time 475 days ≈ 0.754. The bottom horizontal line is $2.0 \times 0.754 - 0.871 \approx 0.637$ (the first plateaux). The first plateaux is of major importance for an outbreak model with contact tracing. The parameter values and initial values are as in Figure 2.

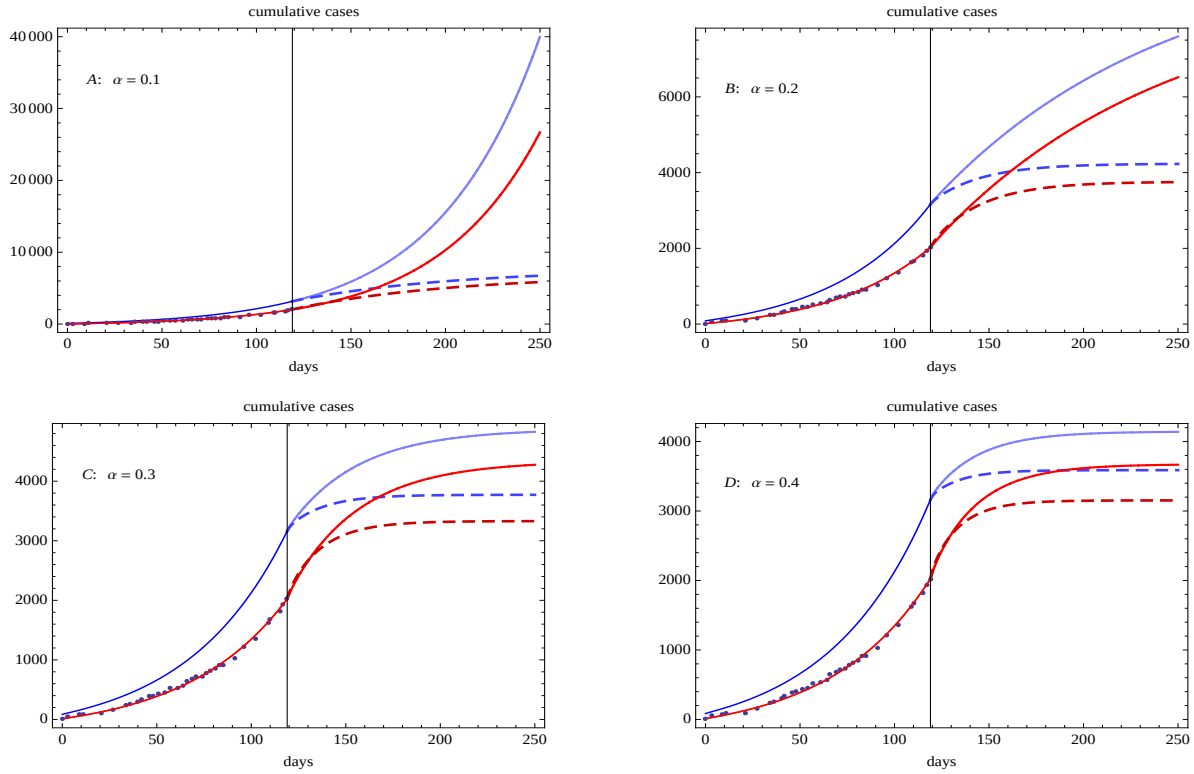

Figure 4: Simulation of predicted cumulative cases in Sierra Leone forward from September 23, 2014 (vertical line). The red graphs are model simulations of reported cases with $\kappa = 0$ (solid), $\kappa = 10$ (dashed). The blue graphs are model simulations of total cases with $\kappa = 0$ (solid), $\kappa = 10$ (dashed). A: $\alpha = 0.1$. B: $\alpha = 0.2$. C: $\alpha = 0.3$. D: $\alpha = 0.4$. The parameter values are is in Figure 2 and $\pi = 0.5$, $\omega = 0.1$. The initial conditions on September 23, 2014 are $S(119) = 5,996,940$, $E(119) = 475$, $I(119) = 191$, $C(119) = 109$.

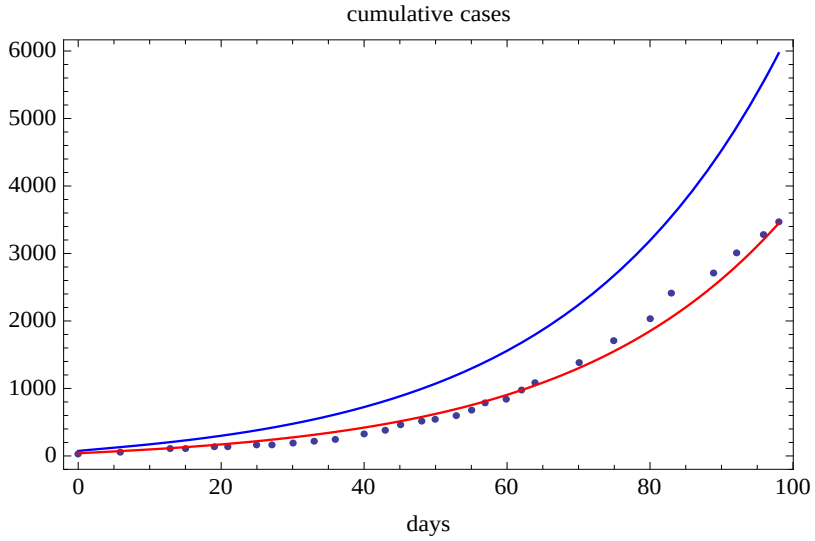

Figure 5: Simulation of the cumulative cases in Liberia from June 17, 2014 to September 23, 2014. The black dots are data of cumulative reported cases (WHO), the red graph is the model simulation of cumulative reported cases, and the blue graph is the model simulation of cumulative total cases. The parameter values are $N = 4,000,000$, $\beta = 0.3$, $\epsilon = 0.316$, $\psi = 0.18$, $\alpha = 0.18$, $\sigma = 1/9$, $\gamma = 1/30$, $\nu = 1/8$, the initial conditions are $S(0) = N$, $E(0) = 40$, $I(0) = 22$, $C(0) = 12$. $\mathcal{R}_0 = 1.54$.

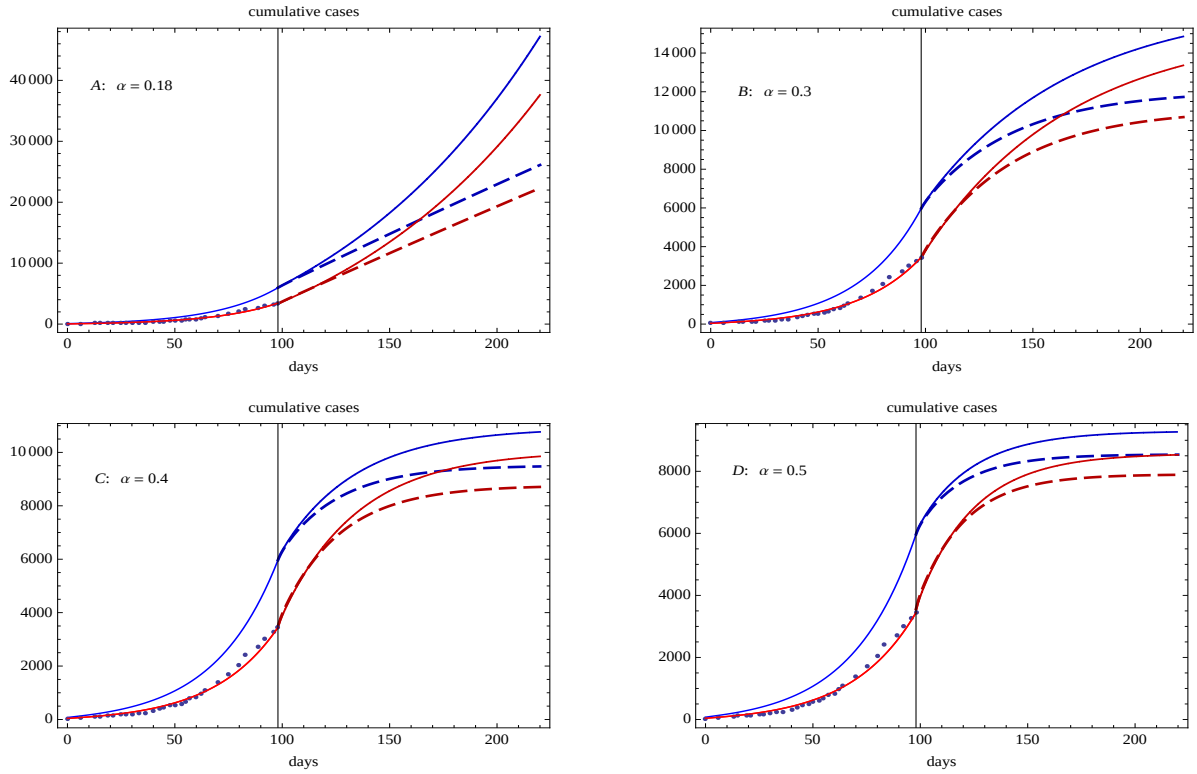

Figure 6: Simulation of predicted cumulative cases in Liberia forward from September 23, 2014 (vertical line). The red graphs are model simulations of reported cases with $\pi = 0.4$ (solid), 0.6 (dashed). The blue graphs are model simulations of total cases with $\pi = 0.4$ (solid), 0.6 (dashed). A: $\alpha = 0.18$. B: $\alpha = 0.3$. C: $\alpha = 0.4$. D: $\alpha = 0.5$. The parameter values are is in Figure 5 and $\kappa = 10$, $\omega = 0.1$. The initial conditions on September 23, 2014 are $S(92) = 3,994,061$, $E(92) = 1544$, $I(92) = 433$, $C(92) = 101$.

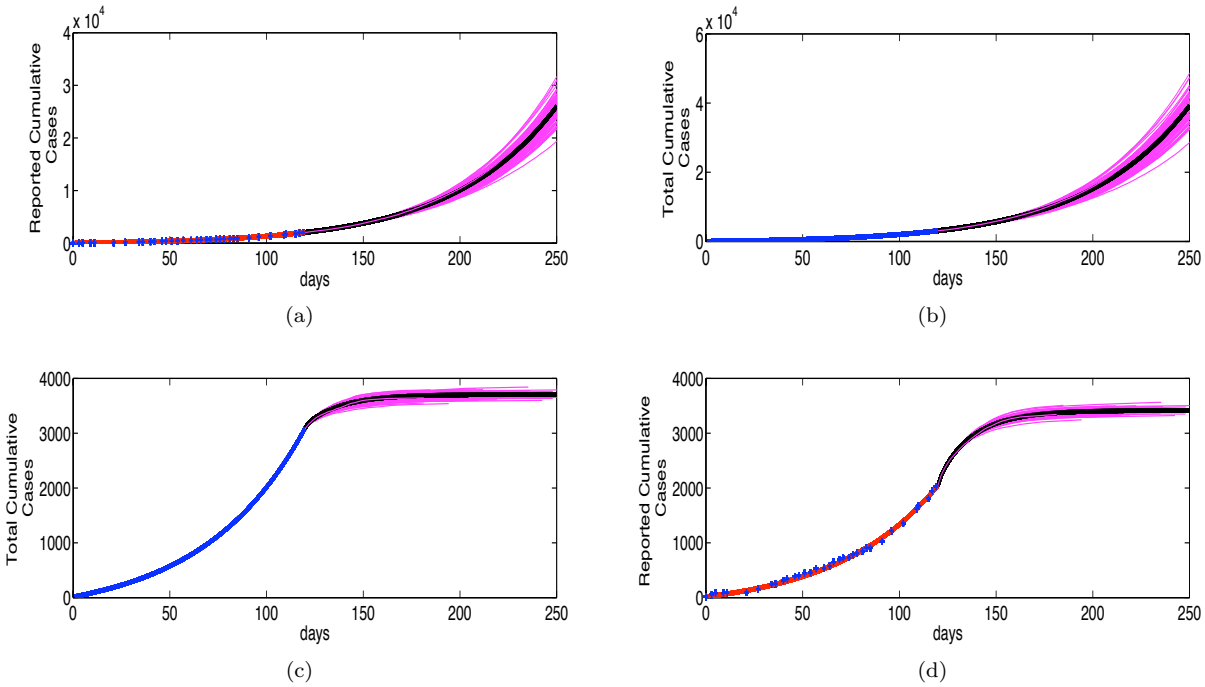

Figure 7: 100 stochastic simulations of predicted cumulative reported cases in Sierra Leone forward from September 23, 2014 with (a) and (b) $\alpha = 0.1$, $\kappa = 0$, and $\alpha = 0.1$, $\kappa = 10$ in (c) and (d). The stochastic simulations are in magenta and the ODE solution is in black. All other parameters are as in Figure 4.