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# Forecasting and Control Policy Assessment for the Ebola Virus Disease (EVD) Epidemic in Sierra Leone Using Small-World Networked Model Simulations

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# Title Page

# Forecasting and Control Policy Assessment for the Ebola Virus Disease (EVD) Epidemic in Sierra Leone Using Small-World Networked Model Simulations

Constantinos I. Siettos[1], Cleo Anastassopoulou[2], Lucia Russo[3], Christos Grigoras[1,4], Eleftherios Mylonakis[4]

**Authors' affiliations:**

[1] School of Applied Mathematics and Physical Sciences, National Technical University of Athens, Athens, Greece.

[2] Division of Genetics, Cell and Developmental Biology, Department of Biology, University of Patras, Patras, Greece.

[3] Consiglio Nazionale di Ricerca, Napoli, Italy.

[4] Division of Infectious Diseases, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI, USA.

**Corresponding author:**

Constantinos I. Siettos: Associate Professor Computational Science & Engineering, School of Applied Mathematics and Physical Sciences, National Technical University of Athens, 9, Heroon Polytechniou Str., GR-157 80 Athens, Greece. Tel.: +30 210-772-3950; E-mail: ksiet@mail.ntua.gr

Eleftherios Mylonakis, M.D., Ph.D., FIDSA, Dean's Professor of Medical Science (Medicine, and Molecular Microbiology and Immunology), Chief, Infectious Diseases Division, Warren Alpert Medical School of Brown University, Rhode Island Hospital 593 Eddy Street, POB, 3rd Floor, Suite 328/330, Providence, RI 02903, Tel: 401-444-7856 / Fax: 401-444-8179.

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## Abstract

**Objectives:** As the Ebola Virus Disease (EVD) still ravages Sierra Leone, we aimed at analyzing the epidemic for the latest period (December 21, 2014 -April 17, 2015) using a small-world networked model and forecast its evolution. Different policy-control scenarios that could lead to the containment of the epidemic were also examined.

**Methods:** We developed a stochastic model with 6.0 million individuals (the population of Sierra Leone) interacting through a small-world social network with adjustable density. The model incorporates the main epidemiologic factors, including the effect of burial practices to virus transmission. The effective reproductive number (*Re)* was also evaluated directly from the individual-based simulations. Estimates of the epidemiologic variables were computed on the basis of the time series of the official cases as reported by the Centers for Disease Control and Prevention (CDC).

**Results:** From December 21, 2014 to February 18, 2015 the epidemic was in recession compared to previous months, as indicated by the estimated effective reproductive number (*Re*) of ~0.77 (95% CI: 0.76-0.78). From February 18 to April 17, 2015 *Re* rose above criticality (~1.98, 95% CI: 1.93-2.02), flashing a note of caution for the situation. Projecting until mid June, we predicted that the epidemic will continue through July. Assessment of different policy-control scenarios showed that the current density of the social network should be reduced by more than 50% to obtain $Re<1$ and contain the epidemic soon.

**Conclusions:** Our results call for an immediate implementation of drastic control measures to contain the epidemic in Sierra Leone.

**Keywords:** EBOV, Sierra Leone, Effective reproductive number, Forecasting, Communicable Disease Control

## Article summary

### Strengths and limitations of this study

- The worst Ebola Virus Disease (EVD) epidemic in history continues to ravage West Africa.
- The mounting concern regarding the continuation of the Ebola Virus Disease (EVD) epidemic in Sierra Leone prompted us to investigate the most recent transmission dynamics of the epidemic in the country.
- While the number of new cases in Sierra Leone seems to decline and schools have reopened for the first time in months, we flash a note of caution for the situation.
- Our analysis reveals that unless drastic control measures are taken immediately, the epidemic is not expected to fade out, but it will continue through July.
- The validity of the analysis depends on the accuracy of the publicly available data. As it has been reported there might be a potential underreporting of the estimated cases and deaths. However even so, the outcome the analysis calls for immediate action.

## Introduction

The worst Ebola Virus Disease (EVD) epidemic in history continues to ravage West Africa. The epidemic began with the report of 49 cases and 29 deaths in Guinea on March 22, 2014 (*1*). Liberia reported its first laboratory-confirmed cases on March 30, 2014, while the first cases in Sierra Leone were reported on May 28, 2014 (*2*). Following regular daily population movements for trade and family visitation, the virus crossed the local porous international borders, establishing chains of transmission not just in small villages, where it would have been easier to contain it, but also in large urban centers. Insufficient public health infrastructure, poor sanitation conditions, lack of education about the disease and unsafe traditional burial practices have also contributed to the spread of the epidemic in the region (*2*).

In Liberia, one of the most affected countries, as of April 20, 2015, a total of 10,042 cases have been recorded, while the toll of death has exceeded 4,480 (*3*). In early March a halt of the epidemic was announced, and even though a new case was confirmed on March 20, 2015, the epidemic is considered to have ceased, while the situation in Sierra Leone is notably different. With more than 12,360 cases and 3,900 deaths until now, Sierra Leone experienced a drop in new cases in January 2015 and authorities loosened mobilization restriction measures to support economic activity (*4*). However, recent WHO updates on the status of the EVD epidemic in this West African nation report a flare up (*3*), with a significant increase among the community of fishermen living in the coastal area of Aberdeen in Freetown (*5*). The synchronous occurrence of over 20 cases suggested they had been infected by a single source, possibly an unsafe burial (*5*).

In light of these recent developments, we analyzed the EVD epidemic dynamics in Sierra Leone for the period between December 21, 2014 and April 17, 2015, using an agent-based, social network model that we reported recently and that proved to provide accurate predictions for the case of Liberia (*6*). For this purpose, the latest official case counts from WHO were fitted to the model, following the so-called Equation-Free approach (*7*). The estimation of key epidemiologic parameters, such as the case fatality rate, the per-contact transmission probability and the mean time from symptoms onset to recovery or to death, allowed us to study the evolving dynamics through the social transmission network whose structure and density are also examined. Through agent-based simulations, we found that the indicative of secondary infections, effective reproductive number (*Re*) was raised above criticality (~1.97, 95% CI: 1.92-2.01) from February 18 to April 17. We thus explored different policy-control scenarios that could lead to reduced *Re* values, and, thereby, to the containment of the epidemic.

## Methods

We developed an individual-based model for the study of the Ebola epidemic (*6*) with $N$ individuals that interact through a Watts & Strogatz (WS) (*8*) small-world network that approximates some attributes of the real social interactions, which are characterized by relatively high clustering and short social distances between them. Here, the network was constructed with the Newman-Watts (*9*) algorithm, in which short-cut edges are added between pairs of nodes with a probability, in the same way as in a WS network, but without removing edges from the underlying lattice. The algorithm starts with a one-dimensional ring network with $k$ local-nearest neighbors per node and with a probability $p_{rw}$ that a link is added between two nodes. Hence, the mean number of additional shortcuts is $p_{rw}\ k\,N$, and the mean total degree of the network is $2\,k\,N\,(1+p_{rw})$. In the constructed small-world network we can adjust the density of the network, say $\alpha$, at will, by randomly adding or subtracting the required number of links.

Agents are categorized in five discrete states: *Susceptible* $(S)$, *Exposed* $(E)$, *Infected* $(I)$, *Dead of the disease but not yet buried* $(D_I)$, and *Dead of the disease and safely buried* $(D_b)$. The $D_I$ infectious state includes agents who die, but whose burial entails risk for onward virus transmission. The transition between states is modeled as a discrete-time, discrete state *non-Markov random process*. Within this framework, the state space over the set of the network links is represented by $Y(\mathbf{V})$, where $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$ is the set of the states of individual $v_k$.

The agent-based rules that govern the dynamics of the epidemic on a daily basis read as follows:

$$p\left(Y_{v_k}(t+1) = D_b \mid Y_{v_k}(t-1) = D_I\right) = 1 \tag{1}$$

$$p\left(Y_{v_k}(t+1) = E \mid Y_{v_l}(t) = I, Y_{v_l}(t) = D_I\right) = p_{s\to E},\ v_l \in \Re_{v_k} \tag{2}$$

$$p\left(Y_{v_k}(t+1) = I \mid Y_{v_k}(t) = E\right) = p_{E\to I} \tag{3}$$

$$p\left(Y_{v_k}(t+1) = D_I \mid Y_{v_k}(t) = I\right) = p_{I\to D} \tag{4}$$

$$p\left(Y_{v_k}(t+1) = R \mid Y_{v_k}(t) = I\right) = p_{I\to R} \tag{5}$$

where $p_{s\to E}$ is the per infected contact transmission probability (still alive or dead, but not yet buried), $p_{E\to I}$, is the inverse of the incubation period, $p_{I\to D}$ is the inverse of the time from symptoms onset to death, $p_{I\to R}$ is the inverse of the recovery period, and, $p_{D/I}$, is the ratio of deaths to the infected population. The rate of the incubation period is taken to be constant, set at $p_{E\to I} = \frac{1}{9}$, as reported by the Who Ebola Response Team (*10*). $\Re_{v_k}$ denotes the neighborhood of an individual $v_k$. This first rule sets the time period from death to burial to two days, during which family members and loved ones may be infected due to physical contact with the dead, still-contagious body. Long-range links of a dead, yet potentially infectious, agent are cut, reflecting the fact that only relatives and close community members can be infected during unsafe funeral practices and rites. The second rule implies that a susceptible agent gets exposed to the disease with a rate determined by the probability $p_{s\to E}$ per infected contact (still alive or dead, but not yet buried). The third rule implies that an exposed agent becomes infectious with a rate determined by the probability $p_{E\to I}$, whose inverse corresponds to the incubation period, i.e. the time from exposure to symptoms onset. Rules (4) and (5) define the case fatality rate, $p_{D/I}$: an agent dies of the disease with a rate determined by the probability $p_{I\to D}$ (whose inverse is the time from symptoms onset to death) (Rule (4)); alternatively, an agent could recover with a rate determined by the probability $p_{I\to R}$ (Rule (5)).

The effective reproductive ratio $R_e$, defined as the average number of secondary infections produced by a typical infective person, is also computed directly from the agent-based simulations.

Based on the demographics reported by the United Nations (UN), the population of Sierra Leone is 6 million (*11*). Time series of the official case counts from the Centers for Disease Control and Prevention (CDC) were used for model fitting (*3*). Case data, which included cumulative incidence and cumulative deaths by date of report for Sierra Leone retrieved on March 19, 2015 were found on (*12*) and compiled from WHO case reports.

Simulations were performed using December 21, 2014 as an initial date and a time horizon of 60 days with an equal sliding window time interval; the last date was April 18, 2015. Thus, fitted values of the network and model parameters, as well as estimates of the effective reproductive ratio, were computed in sequences of succeeded time intervals of 6 weeks corresponding to 2 periods (December 21, 2014 – February 18, 2015 and February 18, 2015 – April 17, 2015). The initial conditions for the starting date of December 21, 2014 were calculated on the basis of agent-based simulations from May 27, 2014, i.e. the date on which the first cases were officially reported from WHO (*2*), following the procedure described in detail elsewhere (*6*). In particular, we obtained the following (expected) numbers for December 21, 2014: $E_0 = 450$, $I_0 = 901$, $D_{b0} = 2390$, $D_{I0} = 28$, $R_0 = 5579$; the estimated cumulative number of cases then was 8,828.

The expected (averaged) values of the agents' states $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$ were computed over $N_r = 8$ network realizations and $N_s = 100$ simulations for each one of the network realizations. The model parameters were fitted to the reported data using a trust-region-reflective approach for nonlinear minimization, implemented for parameter estimation (*13*) exploiting the Equation-Free approach (*7,14-18*). Matlab (*19*) was the simulation environment of choice, while the model was programmed in Fortran 90 and linked to Matlab through mex files.

To forecast the evolution of the Ebola virus epidemic in Sierra Leone, we used the values of the model parameters as estimated in the last period; the resulting parameter values were then fed to the simulator using as coarse initial conditions the values of $\{S, E, I, D_b, D_I, R\}$ as computed on April 17, 2015. We tested the effect of control policy scenarios by reducing the density of the network structure as estimated in the second period. Sparser network densities could reflect partial isolation of the population, restriction of social mobilization combined with an expanded public campaign for increased awareness.

## Results and Discussion

The cumulative numbers of infected and dead obtained by the model compared to the reported cases in Sierra Leone are shown in Figure 1. As shown, our framework succeeds in approximating the actual data for total cases and deaths (*3*). For example, on December 21, 2014 the number of total cases, as reported by the WHO, was 9,004 and the number of deaths was 2,582, while our simulations resulted in 8,828 cases and ~2,400 deaths. On February 18, 2015, the total cases and deaths were 11,103 and 3,408, respectively, and our simulations resulted in 11,049 total cases and 3,394 deaths. Finally, on April 17, 2015, the reported total cases and deaths were 12,244 and 3,865, respectively; our simulations resulted in 12,299 total cases and 3,919 deaths.

The epidemiologic parameters that were obtained through the optimization approach are illustrated in Figure 2 and a summary of the estimated epidemic parameters for the period under study, together with their 95% confidence intervals, is presented in Table 1. Panel (a) depicts the evolution of the estimated network characteristics, $p_{rw}$ and $a$, while panels (b-e) illustrate the model parameters $p_{D/I}$, $p_{I\rightarrow R}$, $p_{I\rightarrow D}$, and $p_{s\rightarrow E}$ that fit best to the reported EVD epidemic dynamics in the country. The evolution of the estimated effective reproductive number $R_e$ in Sierra Leone is shown in panel (f). More specifically, the contact network of Sierra Leone exhibits a rather random structure with a rewiring switching probability ( $p_{rw}$ ) of ~0.37 (95% CI: ~0.33-0.41) that falls down to ~0.22 (95% CI: 0.20-0.24) during the study period (Figure 2a). A slight increase is shown in the density ratio of the network as represented by $a$ , which was ~0.54 (95% CI: ~0.51-0.58) during the first period (December 21, 2014 – February 18, 2015) and ~0.63 (95% CI: 0.59-0.68) during the second period of the study (February 18, 2015 – April 17, 2015) (Figure 2a). The differences of the network characteristics between the 2 periods indicate a more clustered, yet denser contact network during the second period that could partially reflect a relaxation of awareness in the first period, when the epidemic seemed to decline.

The case fatality rate ( $p_{D/I}$ ) that was estimated to be ~32% (95% CI: 31-33%) for the period extending from late December 2014 to February 18 2015, increased to ~39% (95% CI:

38-40%) from February 18 to April 17 (Figure 2b). The expected period from the onset of symptoms to recovery (i.e., the inverse of $p_{I\rightarrow R}$) was ~9.5 days (95% CI: 8.6-10.7 days) during the first period and ~8 days (95% CI: 6.5-10.5 days)for the second period of study (Figure 2c). The expected period from the onset of symptoms to death (i.e., the inverse of $p_{I\rightarrow D}$) was constant at ~3.6 days (95% CI: 3.3-4.0 days) during the period of study (Figure 2d).

Regarding the epidemic parameters, our estimates are quite close to the ones reported by the WHO Ebola Response Team and other groups. For example, Ansumana et al. (*20*) reported a 31% CFR at Hastings center, while the National Institute of Communicable diseases (NICD) reports a CFR of 32% for Sierra Leone on April 5, 2015 (*21*); a mean of 31.6% CFR was reported for Sierra Leone from the WHO Ebola response team as of September 14, 2014 (*10*). Gomes et al. (*22*) reported an ~8 day-period from the onset of symptoms to recovery, while in a recent study by the WHO Ebola response team (*23*) a period of 10.6 days (with a SD of 8.2 days) was reported from symptoms onset to hospital discharge for individuals of older than 45 years old. In the same paper, a period of ~6 days (with equal SD) is reported from symptoms onset to death for the same age group. The same delay period from symptoms onset to death was also reported in Ansumana et al. (*20*).

The per-contact transmission probability $p_{s\rightarrow E}$ values were estimated at ~0.03 (95% CI: 0.028-0.033) in the first period and ~0.08 (95% CI: 0.067-0.09) in the second period (Figure 2e). Finally, the effective reproductive number $R_e$, as computed using the agent-based simulator, was ~0.77 (95% CI: 0.76-0.78) from December 21, 2014 to February 18, 2015, rising up to ~1.98 (95% 1.93-2.02) from February18, 2015 to April 17, 2015 (Figure 2f).

Simulations show that the expected cumulative number of infected cases may reach as high as 13,400 by mid of June, while the cumulative number of dead may reach 4,380, if no further action is undertaken. Hence, we decided to perform an assessment of the impact of potential control strategies. Based on the recently announced isolation policy (*24*), we simulated the influence on the epidemic dynamics of sparser, with respect to the estimated network density of the second period, network densities, by 10%, 20%, 30%, 40% and 50%. We tested these scenarios by reducing analogously the expected density of the contact network as estimated during the second period and running the agent-based simulation from April 18 until mid of June 2015, keeping all other values of the model parameters fixed.

The results of the exploration of these different scenarios are summarized in Table 2 and portrayed graphically in Figure 3. The "no further action" case, with respect to the estimated current network structure is also depicted in Figure 3 for comparison. By applying a 10% reduction in the network density (yielding an $a$ of ~0.57), the expected reproductive number $R_e$ was estimated to be ~1.7. Accordingly, for a 20% reduction in the network density (yielding an $a$ of ~0.51), $R_e$ was estimated to be ~1.51. Reductions of 30%, 40% and 50% yielding network densities of ~0.44 , ~0.38 and ~0.32 respectively, resulted in $R_e$ values of ~1.42, ~1.23 and ~1.05 correspondingly (Table 2). As is shown even large reductions in the density of the network will not lower the $R_e$ below unity soon.

In reality, the reduction in the network density could potentially reflect analogous reductions in social interactions further to the current restrictions of community mobilization. Examples would include raising public awareness and/or strengthening medical care. The country's National Ebola Response Centre has already announced a 3-day lockdown that will affect around 2.5 million people (*20*). Nevertheless, it is worth noticing that even with a 30% reduction in the social network density, the epidemic shows no signs of fading out until the mid of June and we estimate that new cases will continue to be recorded.

In conclusion, we found that the EVD epidemic in Sierra Leone was in recession in the period between December 21, 2014 through mid of February, 2015, as reflected by the

<1 value of the reproductive number for this period. However, during the last period (i.e., from February 18 to April 17, 2015), the epidemic has spiked and the reproductive number was estimated to be well above criticality, with the potential to persist at this level beyond the end of June and through July. Control measures associated with mobilization restrictions were also evaluated. Our findings, supported by real epidemiologic data and the projection of a spilling over of the epidemic to mid of June, indicate that the measures implemented so far are inadequate. Taken in their totality, these findings indicate that the epidemic, even with strict control isolation policies in effect, will go on through July with a probability of fading out thereafter if policies are implemented and consistently kept in place. Immediate, more intense efforts are needed before further complications emerge. Reducing the effective density of the derived contact small-world-like network, through limited social interactions, has the potential to improve the current situation.

## Contributorship statement

Constantinos Siettos, Lucia Russo and Christos Grigoras contributed to the development of the model. Constantinos Siettos and Cleo Anastassopoulou contributed to the data collection, interpretation of the data and drafting the paper. Eleftherios Mylonakis contributed to the interpretation of the data and substantially revised the paper. All authors approved the final manuscript and accepted accountability for all aspects of the work.

## Competing interests

There are no competing interests.

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## Data Sharing Statement

The data used in this study are publicly available from CDC at http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/

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**Table 1.** Key epidemiologic features of the Ebola Virus Disease (EVD) epidemic in Sierra Leone estimated by the model during the first and second study period (December 21, 2014 - April 17, 2015).

| | | **Sierra Leone** | |
|---|---|---|---|
| **Period** | **Variable** | **Mean** | **95% CI** |
| **First**<br>(Dec. 21-<br>Feb. 18, 2015) | $p_{rw}$ | 0.37 | 0.33-0.41 |
| | Network density (α) | 0.55 | 0.51-0.58 |
| | Time to death (Days) | 3.6 | 3.3-4.0 |
| | Time to recovery (Days) | 9.5 | 8.6-10.7 |
| | CFR (%) | 32 | 31-33 |
| | $R_e$ | 0.77 | 0.76-0.78 |
| **Second**<br>(Feb. 18-April.<br>17, 2015) | $p_{rw}$ | 0.22 | 0.20-0.24 |
| | Network density (α) | 0.63 | 0.59-0.68 |
| | Time to death (Days) | 3.6 | 3.3-4.0 |
| | Time to recovery (Days) | 8.0 | 6.5-10.5 |
| | CFR (%) | 39 | 38-40 |
| | $R_e$ | 1.98 | 1.93-2.02 |

$p_{rw}$, Rewiring switching probability; CFR, Case fatality rate ( $p_{D/I}$ ); $R_e$, Effective reproductive number

**Table 2.** Outcomes of isolation control policy scenarios on the basis of the expected reproductive number $R_e$, as computed by running the agent-based simulation from April 17 to the mid of June 2015 (keeping fixed all other values of the model parameters). Sparser density refers to a percent reduction of the expected density of the contact network compared to the 0.63 value that was estimated for the second period (February 18 – April 17, 2015).

| **Period** | **% Sparser density** | **Network density** (α) | $R_e$ |
|---|---|---|---|
| (April 7-June, 17, 2015) | 10% | ~0.57 | ~1.7 |
| | 20% | ~0.51 | ~1.5 |
| | 30% | ~0.44 | ~1.4 |
| | 40% | ~0.38 | ~1.2 |
| | 50% | ~0.32 | ~1.0 |

## FIGURE LEGENDS

**Figure 1. Simulation Results for Sierra Leone from December 21, 2014 to April 17, 2015.** Expected cumulative cases of infected (dotted red) and dead (dotted black). WHO data are depicted by solid lines. The period under study has been tessellated into two windows with a length of 60 days each. For each window, the model parameters are estimated based on the data reported from WHO.

**Figure 2. Estimated model parameters for Sierra Leone from December 21, 2014 to April 17, 2015. (a)** Evolution of contact network characteristics: switching probability ($p_{rw}$) and density ratio of the transmission network ($a$). **(b)** Case fatality rate ($p_{D/I}$). **(c)** 1/{recovery period} ($p_{I \to R}$). **(d)** 1/{period from inset of symptoms to death} ($p_{I \to D}$). **(e)** Per-contact transmission probability ($p_{s \to E}$). **(f)** Effective reproductive number ($R_e$). 95% Confidence intervals are also shown.

**Figure 3. Forecasting of the evolution of the epidemic from April, 17 to June 17, 2015 under different control scenarios**. Network density values were compared to the density of the social network estimated for the period February 18-April 17, 2015. **(a)** Total Cases, **(b)** Deaths. The “no further action” scenario is also depicted.

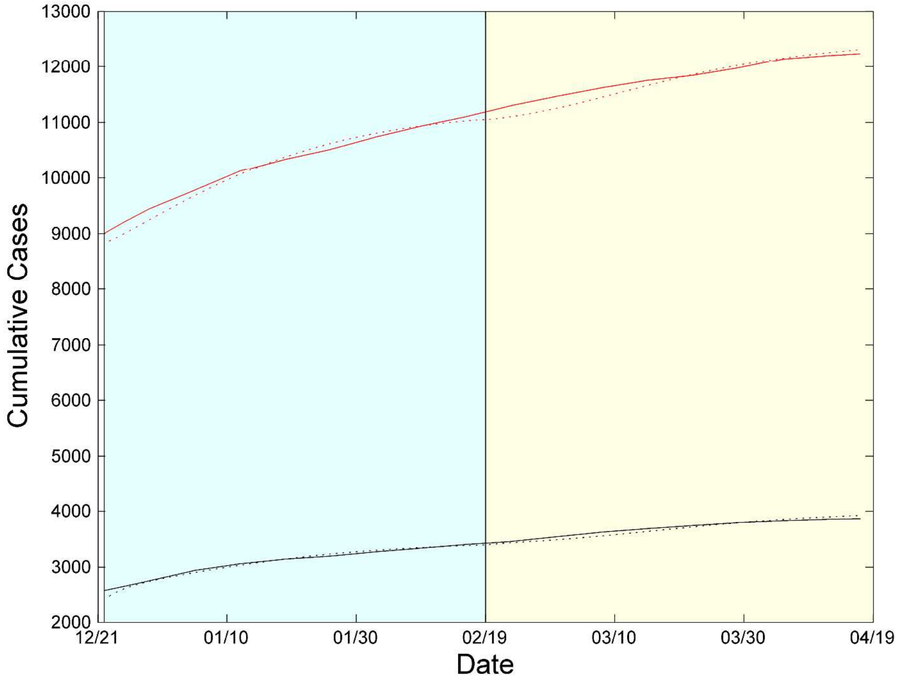
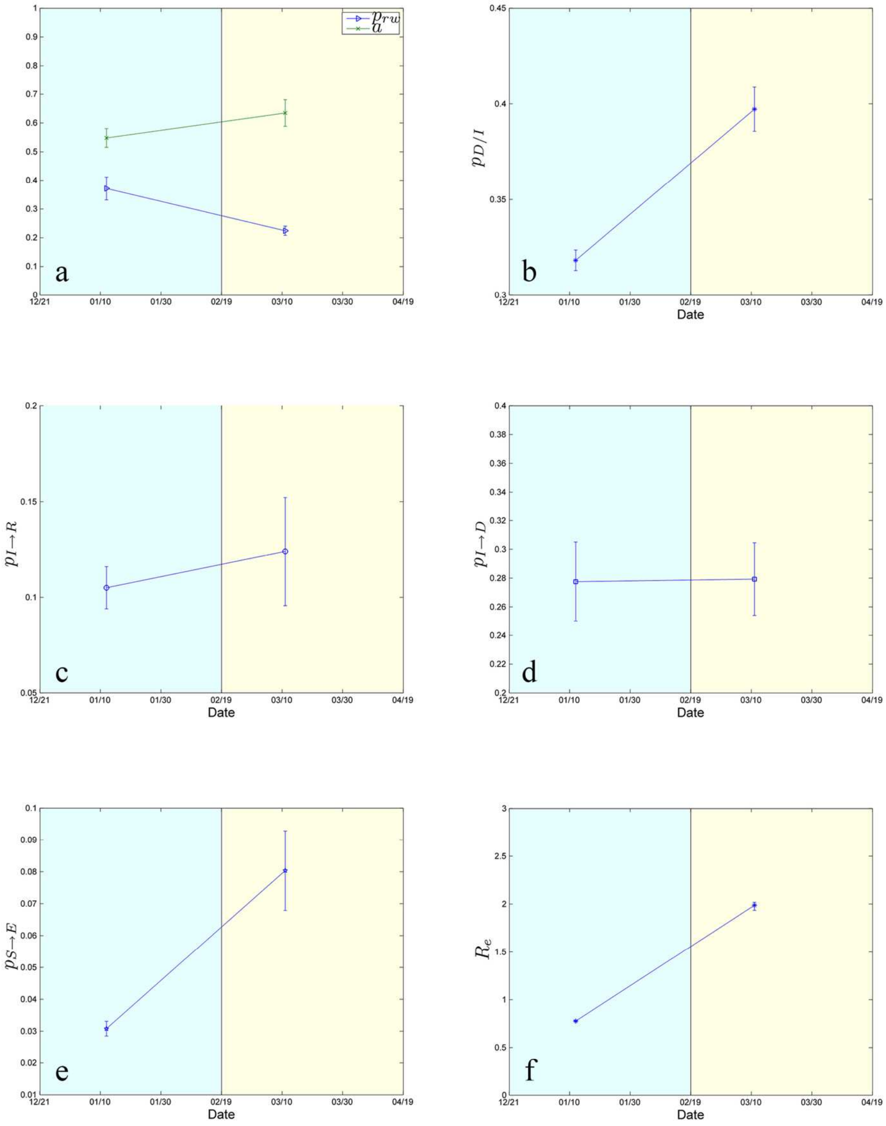


Figure 1. Simulation Results for Sierra Leone from December 21, 2014 to April 17, 2015. Expected cumulative cases of infected (dotted red) and dead (dotted black). WHO data are depicted by solid lines. The period under study has been tessellated into two windows with a length of 60 days each. For each window, the model parameters are estimated based on the data reported from WHO.



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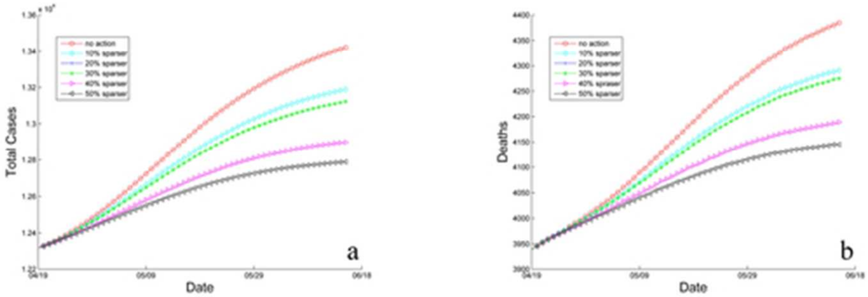

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# Forecasting and Control Policy Assessment for the Ebola Virus Disease (EVD) Epidemic in Sierra Leone Using Small-World Networked Model Simulations

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# Title Page

# Forecasting and Control Policy Assessment for the Ebola Virus Disease (EVD) Epidemic in Sierra Leone Using Small-World Networked Model Simulations

Constantinos I. Siettos[1], Cleo Anastassopoulou[2], Lucia Russo[3], Christos Grigoras[1,4], Eleftherios Mylonakis[4]

**Authors' affiliations:**
[1] School of Applied Mathematics and Physical Sciences, National Technical University of Athens, Athens, Greece.
[2] Division of Genetics, Cell and Developmental Biology, Department of Biology, University of Patras, Patras, Greece.
[3] Consiglio Nazionale di Ricerca, Napoli, Italy.
[4] Division of Infectious Diseases, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI, USA.

**Corresponding author:**

Constantinos I. Siettos: Associate Professor Computational Science & Engineering, School of Applied Mathematics and Physical Sciences, National Technical University of Athens, 9, Heroon Polytechniou Str., GR-157 80 Athens, Greece. Tel.: +30 210-772-3950; E-mail: ksiet@mail.ntua.gr

Eleftherios Mylonakis, M.D., Ph.D., FIDSA, Dean's Professor of Medical Science (Medicine, and Molecular Microbiology and Immunology), Chief, Infectious Diseases Division, Warren Alpert Medical School of Brown University, Rhode Island Hospital 593 Eddy Street, POB, 3rd Floor, Suite 328/330, Providence, RI 02903, Tel: 401-444-7856 / Fax: 401-444-8179.

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## Abstract

**Objectives:** As the Ebola Virus Disease (EVD) is still sustained in Sierra Leone, we analyzed the epidemic for the latest period (December 21, 2014 -April 17, 2015) using a small-world networked model and forecasted its evolution. Policy-control scenarios for the containment of the epidemic were also examined.

**Methods:** We developed an agent-based model with 6 million individuals (the population of Sierra Leone) interacting through a small-world social network. The model incorporates the main epidemiologic factors, including the effect of burial practices to virus transmission. The effective reproductive number (*Re)* was evaluated directly from the agent-based simulations. Estimates of the epidemiologic variables were computed on the basis of the official cases as reported by the Centers for Disease Control and Prevention (CDC).

**Results:** From December 21, 2014 to February 18, 2015 the epidemic was in recession compared to previous months, as indicated by the estimated effective reproductive number (*Re*) of ~0.77 (95% CI: 0.72-0.82). From February 18 to April 17, 2015, *Re* rose above criticality (~1.98, 95% CI: 1.33-2.22), flashing a note of caution for the situation. By projecting in time, we predicted that the epidemic would continue through July 2015. Our predictions were close to the cases reported by CDC by the end of June, verifying the criticality of the situation. In light of these developments, while revising our manuscript, we expanded our analysis to include the most recent data (until August 15, 2015). By mid-August, *Re* has fallen below criticality and the epidemic is expected to fade out by early December 2015.

**Conclusions:** Our results call for the continuation of drastic control measures, which in the absence of an effective vaccine or therapy at present can only translate to isolation of the infected section of the population, to contain the epidemic.

**Keywords:** EBOV, Sierra Leone, Effective reproductive number, Forecasting, Communicable Disease Control, Agent-Based Modeling, Social Transmission Network

## Article summary

### Strengths and limitations of this study

- The greatest strength of this study stems from the undertaken mathematical approach of choice, integrating agent-based modeling on complex networks and the so-called Equation-Free approach, which allowed us to assess various important epidemiologic parameters and to obtain accurate short-term forecasts of the evolution of the Ebola Virus Disease (EVD) epidemic in Sierra Leone.
- Another advantage of the proposed methodology is that it allows for the rapid evaluation of different policy-control scenarios that could lead to the containment of the epidemic.
- Our predictions were verified by the official case count reported by CDC. An updated analysis considering data until mid August shows that the epidemic is expected to fade out by early December 2015.
- The validity of a modeling analysis depends on the accuracy of input data. The most important limitation of our study pertains to the quality and accuracy of the outbreak data that were “fed” to the mathematical model compared to the real figures. Underreporting of cases and deaths is certainly to be expected under the particular circumstances of such a severe epidemic evolving in one of the most impoverished countries in the world. However, even so, the outcome the analysis calls for the continuation of control measures to contain the epidemic.

## Introduction

The worst Ebola Virus Disease (EVD) epidemic in history continues to ravage West Africa. The epidemic began with the report of 49 cases and 29 deaths in Guinea on March 22, 2014 (*1*). Liberia reported its first laboratory-confirmed cases on March 30, 2014, while the first cases in Sierra Leone were reported on May 28, 2014 (*2*). Following regular daily population movements for trade and family visitation, the virus crossed the local porous international borders, establishing chains of transmission not just in small villages, where it would have been easier to contain it, but also in large urban centers. Insufficient public health infrastructure, poor sanitation conditions, lack of education about the disease and unsafe traditional burial practices have also contributed to the spread of the epidemic in the region (*2*).

In Liberia, one of the most affected countries, as of April 20, 2015, a total of 10,042 cases have been recorded, while the toll of death has exceeded 4,480 (*3*). In early March a halt of the epidemic was announced, and even though a new case was confirmed on March 20, 2015, the epidemic is considered to have ceased, while the situation in Sierra Leone is notably different. With more than 12,360 cases and 3,900 deaths until now, Sierra Leone experienced a drop in new cases in January 2015 and authorities loosened mobilization restriction measures to support economic activity (*4*). However, recent World Health Organization WHO updates on the status of the EVD epidemic in this West African nation report a flare up (*3*), with a significant increase among the community of fishermen living in the coastal area of Aberdeen in Freetown (*5*). The synchronous occurrence of over 20 cases suggested they had been infected by a single source, possibly an unsafe burial (*5*).

In light of these recent developments, we analyzed the EVD epidemic dynamics in Sierra Leone for the period between December 21, 2014 and April 17, 2015, using an agent-based, social network model that we reported recently and that proved to provide accurate predictions for the case of Liberia (*6*). For this purpose, the latest official case counts from WHO were fitted to the model, following the so-called Equation-Free approach (*7*). Our objective was to obtain estimates of key epidemiologic parameters, such as the case fatality rate, the per-contact transmission probability and the mean time from symptoms onset to recovery or to death, in order to study the evolving dynamics through the social transmission network whose structure and density are also examined. Through agent-based simulations, we found that the indicative of secondary infections, effective reproductive number (*Re*) was raised above criticality (~1.97, 95% CI: 1.92-2.01) from February 18 to April 17, 2015. We thus explored different policy-control scenarios that could lead to reduced *Re* values, and, thereby, to the containment of the epidemic. While revising our manuscript, we also processed the reported data from CDC of the very last period (April 18-August 15, 2015), obtaining more optimistic estimates indicative of a remission of the epidemic in Sierra Leone, as reflected by the derived $R_e$ for the period June 17-August 15, 2015 (~0.68, 95% CI: 0.49-1.01). Projecting from August 15, we estimate that the epidemic will fade out in early December.

## Methods

We developed an agent-based model for the study of the Ebola epidemic (*6*) with $N$ individuals that interact through a Watts & Strogatz (WS) (*8*) small-world network that approximates some attributes of the real social interactions, which are characterized by relatively high clustering and short social distances between them. Here, the network was constructed with the Newman-Watts (*9*) algorithm, in which short-cut edges are added between pairs of nodes with a probability, in the same way as in a WS network, but without removing edges from the underlying lattice. The algorithm starts with a one-dimensional ring network with $k$ local-nearest neighbors per node and with a probability $p_{rw}$ that a link is added between two nodes. Hence, the mean number of additional shortcuts is $p_{rw}\, k\, N$, and the mean total degree of the network is $2\,k\,N\,(1+p_{rw})$. In the constructed small-world network we can adjust the density of the network, say $\alpha$, at will, by randomly adding or subtracting the required number of links.

Agents are categorized in five discrete states: *Susceptible* $(S)$, *Exposed* $(E)$, *Infected* $(I)$, *Dead of the disease but not yet buried* $(D_I)$, *Dead of the disease and safely buried* $(D_b)$, and *Recovered (R)* (*6*). The $D_I$ infectious state includes agents who die, but whose burial entails risk for onward virus transmission. The transition between states is modeled as a discrete-time, discrete state *non-Markov random process*. Within this framework, the state space over the set of the network links is represented by $Y(\mathbf{V})$, where $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$ is the set of the states of individual $v_k$.

The agent-based rules that govern the dynamics of the epidemic on a daily basis read as follows:

$$p\left(Y_{v_k}(t+1)=D_b \mid Y_{v_k}(t-1)=D_I\right)=1 \qquad (1)$$

$$p\left(Y_{v_k}(t+1)=E \mid Y_{v_l}(t)=I, Y_{v_l}(t)=D_I\right)=p_{s\to E},\ v_l \in \Re_{v_k} \qquad (2)$$

$$p\left(Y_{v_k}(t+1)=I \mid Y_{v_k}(t)=E\right)=p_{E\to I} \qquad (3)$$

$$p\left(Y_{v_k}(t+1)=D_I \mid Y_{v_k}(t)=I\right)=p_{I\to D} \qquad (4)$$

$$p\left(Y_{v_k}(t+1)=R \mid Y_{v_k}(t)=I\right)=p_{I\to R} \qquad (5)$$

where $p_{s\to E}$ is the per infected contact transmission probability (still alive or dead, but not yet buried), $p_{E\to I}$, is the inverse of the incubation period, $p_{I\to D}$ is the inverse of the time from symptoms onset to death, $p_{I\to R}$ is the inverse of the recovery period, and, $p_{D/I}$, is the ratio of deaths to the infected population (*6*). The rate of the incubation period is taken to be constant, set at $p_{E\to I}=\frac{1}{9}$, as reported by the Who Ebola Response Team (*10*). $\Re_{v_k}$ denotes the neighborhood of an individual $v_k$. This first rule sets the time period from death to burial to two days, during which family members and loved ones may be infected due to physical contact with the dead, still-contagious body. Long-range links of a dead, yet potentially infectious, agent are cut, reflecting the fact that only relatives and close community members can be infected during unsafe funeral practices and rites. The second rule implies that a susceptible agent gets exposed to the disease with a rate determined by the probability $p_{s\to E}$ per infected contact (still alive or dead, but not yet buried). The third rule implies that an exposed agent becomes infectious with a rate determined by the probability $p_{E\to I}$, whose inverse corresponds to the incubation period, i.e. the time from exposure to symptoms onset. Rules (4) and (5) define the case fatality rate, $p_{D/I}$: an agent dies of the disease with a rate determined by the probability $p_{I\to D}$ (whose inverse is the time from symptoms onset to death) (Rule (4)); alternatively, an agent could recover with a rate determined by the probability $p_{I\to R}$ (Rule (5)).

The effective reproductive ratio $R_e$, defined as the average number of secondary infections produced by a typical infective person, is also computed directly from the agent-based simulations.

Based on the demographics reported by the United Nations (UN), the population of Sierra Leone is 6 million (*11*). Time series of the official Ebola case counts from the Centers for Disease Control and Prevention (CDC) were used for model fitting (*3*). These case counts were collected from public data released by the World Health Organization (WHO) (*12*) and CDC (3). Even though these data sets do not distinguish between suspect, probable and laboratory-confirmed case counts, they are considered to represent the best available estimates of the current state of the epidemic in the severely afflicted West African countries. Case data, which included cumulative incidence and cumulative deaths by date of report for Sierra Leone, were retrieved on April 24, 2015.

Simulations were performed using December 21, 2014 as an initial date and a time horizon of 60 days with an equal sliding window time interval; the last date was April 17, 2015. Thus, fitted values of the network and model parameters, as well as estimates of the effective reproductive ratio, were computed in sequences of succeeded time intervals of 60 days corresponding to 2 periods (December 21, 2014 – February 18, 2015 and February 18, 2015 – April 17, 2015). The initial conditions for the starting date of December 21, 2014 were calculated on the basis of agent-based simulations from May 27, 2014, i.e. the date on which the first cases were officially reported from WHO (*2*), following the procedure described in detail elsewhere (*6*). In particular, we obtained the following (expected) numbers for December 21, 2014: $E_0 = 450$, $I_0 = 901$, $D_{b0} = 2390$, $D_{I0} = 28$, $R_0 = 5579$; the estimated cumulative number of cases then was 8,828.

The expected (averaged) values of the agents' states $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$ were computed over $N_r = 8$ network realizations and $N_s = 100$ simulations for each one of the network realizations. The model parameters were fitted to the reported data using a trust-region-reflective approach for nonlinear minimization, implemented for parameter estimation (*13*) exploiting the Equation-Free approach (*7,14-18*). Matlab (*19*) was the simulation environment of choice, while the model was programmed in Fortran 90 and linked to Matlab through mex files.

To forecast the evolution of the Ebola virus epidemic in Sierra Leone, we used the values of the model parameters as estimated in the last period; the resulting parameter values were then fed to the simulator using as coarse initial conditions the values of $\{S, E, I, D_b, D_I, R\}$ as computed on April 17, 2015. We tested the effect of control policy scenarios by reducing the density of the network structure as estimated in the second period. Sparser network densities could reflect partial isolation of the population, restriction of social mobilization combined with an expanded public campaign for increased awareness.

## Results and Discussion

The cumulative numbers of infected and dead obtained by the model compared to the reported cases in Sierra Leone are shown in Figure 1. Our framework succeeds in approximating the actual data for total cases and deaths (*3*). For example, on December 21, 2014 the number of total cases, as reported by the WHO, was 9,004 and the number of deaths was 2,582, while our simulations resulted in 8,828 cases and ~2,400 deaths. On February 18, 2015, the total cases and deaths were 11,103 and 3,408, respectively, and our simulations resulted in 11,049 total cases and 3,394 deaths. Finally, on April 17, 2015, the reported total cases and deaths were 12,244 and 3,865, respectively; our simulations resulted in 12,299 total cases and 3,919 deaths.

The epidemiologic parameters that were obtained through the optimization approach are illustrated in Figure 2 and a summary of the estimated epidemic parameters for the period under study, together with their 95% confidence intervals, is presented in Table 1. Panel (a) depicts the evolution of the estimated network characteristics, $p_{rw}$ and $a$, while panels (b-e) illustrate the model parameters $p_{s\to E}$, $p_{D/I}$, $p_{I\to R}$ and $p_{I\to D}$ that fit best to the reported EVD epidemic dynamics in the country. The evolution of the estimated effective reproductive number $R_e$ in Sierra Leone is shown in panel (f). More specifically, the contact network of Sierra Leone exhibits a rather random structure with a rewiring switching probability ($p_{rw}$) of ~0.37 (95% CI: ~0.33-0.41) that falls down to ~0.22 (95% CI: 0.20-0.24) during the study period (Figure 2a). A slight increase is shown in the density ratio of the network as represented by $a$, which was ~0.54 (95% CI: ~0.51-0.58) during the first period (December 21, 2014 – February 18, 2015) and ~0.63 (95% CI: 0.59-0.68) during the second period of the study (February 18, 2015 – April 17, 2015) (Figure 2a). The differences of the network characteristics between the two periods indicate a more clustered, yet denser contact network during the second period that could partially reflect a relaxation of awareness in the first period, when the epidemic seemed to decline.

The case fatality rate ($p_{D/I}$) that was estimated to be ~32% (95% CI: 31-33%) for the period extending from late December 2014 to February 18 2015, increased to ~39% (95% CI: 38-40%) from February 18 to April 17 (Figure 2e). The expected period from the onset of symptoms to recovery (i.e., the inverse of $p_{I\to R}$) was ~9.5 days (95% CI: 8.6-10.7 days) during the first period and ~8 days (95% CI: 6.5-10.5 days) for the second period of study (Figure 2c). The expected time interval from the onset of symptoms to death (i.e., the inverse of $p_{I\rightarrow D}$ ) was constant at ~3.6 days (95% CI: 3.3-4.0 days) during the period of study (Figure 2d).

Regarding the epidemic parameters, our estimates are quite close to the ones reported by the WHO Ebola Response Team and other groups. For example, Ansumana *et al*. (*20*) reported a 31% CFR at Hastings center, while the National Institute of Communicable diseases (NICD) reports a CFR of 32% for Sierra Leone on April 5, 2015 (*21*); a mean of 31.6% CFR was reported for Sierra Leone from the WHO Ebola response team as of September 14, 2014 (*10*). Gomes *et al*. (*22*) reported an ~8 day-period from the onset of symptoms to recovery, while in a recent study by the WHO Ebola response team (*23*) a period of 10.6 days (with a SD of 8.2 days) was reported from symptoms onset to hospital discharge for individuals of older than 45 years old. In the same paper, a period of ~6 days (with equal SD) is reported from symptoms onset to death for the same age group. The same delay period from symptoms onset to death was also reported in Ansumana *et al*. (*20*).

The per-contact transmission probability $p_{s\rightarrow E}$ values were estimated at ~0.03 (95% CI: 0.028-0.033) in the first period and ~0.08 (95% CI: 0.067-0.09) in the second period (Figure 2b). Finally, the effective reproductive number $R_e$, as computed using the agent-based simulator, was ~0.77 (95% CI: 0.72-0.82) from December 21, 2014 to February 18, 2015, rising up to ~1.98 (95% 1.33-2.22) from February18, 2015 to April 17, 2015 (Figure 2f).

Simulations show that the expected cumulative number of infected cases may reach as high as 13,400 by June 17, while the cumulative number of dead may exceed 4,300, if no further action is undertaken. Hence, we decided to perform an assessment of the impact of potential control strategies. Based on the recently announced isolation policy (*24*), we simulated the influence on the epidemic dynamics of sparser, with respect to the estimated network density of the second period, network densities, by 10%, 20%, 30%, 40% and 50%. We tested these scenarios by reducing analogously the expected density of the contact network as estimated during the second period and running the agent-based simulation from April 18 until June17, 2015, keeping all other values of the model parameters fixed.

The results of the exploration of these different scenarios are summarized in Table 2 and portrayed graphically in Figure 3. The "no further action" case, with respect to the estimated current network structure is also depicted in Figure 3 for comparison. By applying a 10% reduction in the network density (yielding an $a$ of ~0.57), the expected reproductive number $R_e$ was estimated to be ~1.7. Accordingly, for a 20% reduction in the network density (yielding an $a$ of ~0.51), $R_e$ was estimated to be ~1.51. Reductions of 30%, 40% and 50% yielding network densities of ~0.44, ~0.38 and ~0.32 respectively, resulted in $R_e$ values of ~1.42, ~1.23 and ~1.05 correspondingly (Table 2). As shown, even large reductions in the density of the network will not lower the $R_e$ below unity soon.

A study by Khan *et al*. that obtained robust estimates for the basic reproductive ratio $R_0$ in both Liberia and Sierra Leone showed that effective isolation is required to bring the value of $R_0$ to less than 1, and hence control the outbreak (*25*). Khan *et al*. suggested that the contact rate in isolation should be less than one quarter of that for the infected non-isolated population, and that, the fraction of high-risk individuals should be brought to less than 10% of the overall susceptible population, to halt the epidemic (*25*).

In reality, the reduction in the network density could potentially reflect analogous reductions in social interactions further to the current restrictions of community mobilization. Examples would include raising public awareness and/or strengthening medical care. The country's National Ebola Response Centre has already announced a 3-day lockdown that will affect around 2.5 million people (*20*). Nevertheless, it is worth noticing that even with a 30% reduction in the social network density, the epidemic shows no signs of fading out until June 17 and we estimate that new cases will continue to be recorded.

In conclusion, we found that the EVD epidemic in Sierra Leone was in recession in the period between December 21, 2014 through mid-February, 2015, as reflected by the <1 value of the reproductive number for this period. However, during the second study period (i.e., from February 18 to April 17, 2015), the epidemic has spiked and the reproductive number was estimated to be well above criticality, with the potential to persist at this level beyond the end of June and through July. Control measures associated with mobilization restrictions were also evaluated. Our findings, supported by real epidemiologic data and the projection of a spilling over of the epidemic to mid-June, indicate that the measures implemented so far are inadequate. Taken in their totality, these findings indicate that the epidemic, even with strict control isolation policies in effect, will go on through July with a probability of fading out thereafter if policies are implemented and consistently kept in place. Immediate, more intense efforts are needed before further complications emerge. Reducing the effective density of the derived contact small-world-like network, through limited social interactions, has the potential to improve the current situation. Our results and predictions were verified from the official data reported by CDC for the corresponding period of study. Hence, our approach seems promising to forecast re-emergent outbreaks in other vulnerable regions of Africa, such as Eastern and Central Africa, where Ebola outbreaks have traditionally occurred in the past. Estimations through clinical studies of important factors such as the contact transmission probability, mortality and recovery rate, incubation periods as well as detailed age-specific data as the epidemic develops in space and time, would enhance our ability to better model, forecast and design efficient control policies.

However, the usefulness of mathematical models should not be overestimated. Despite the significant technological progress and concentrated wealth, breakdowns and cuts in public health infrastructures worldwide are (the) major reasons for boosting epidemics. Liberia and Sierra Leone, the two countries that have been worst affected from the Ebola epidemic had an almost non-existent health care system: as reported Liberia with a population of more than 4 million people had just 51 physicians and Sierra Leone with a population exciting 6 million had just 136 physicians (26).

### *Update to the case of Sierra Leone (period April 18-August 15, 2015)*

Since the results we obtained by analyzing the reported data until April 17, 2015 showed that the epidemic was sustained in Sierra Leone, we decided to investigate further the current trends of the epidemic dynamics. Therefore, we expanded our analysis by taking into account the reported data for the country for the very last period (April 18-August 15, 2015). The results of this expanded analysis indicate a declining trend in the transmission potential of the virus, as shown in Table 3. More specifically, ( $p_{rw}$ ) rose significantly in the period April 18-June 16, 2015 to ~0.69 (95% CI: ~0.67-0.72) with a further slight increase in the very last period (June 17-August 15, 2015) to ~0.75 (95% CI: 0.69-0.80). The density ratio of the network as represented by $a$ , did not show significant changes: in the period April 18-June 16, 2015 it was found to be ~0.47 (95% CI: ~0.42-0.51) and ~0.46 (95% CI: 0.37-0.53) during the period June 17-August 15, 2015. The case fatality rate ( $p_{D/I}$ ) dropped to ~10% (95% CI: 8-12%) for both last periods. The expected period from the onset of symptoms to recovery (i.e., the inverse of $p_{I\to R}$ ) was ~20 days (95% CI: 16-30 days) during the period April 18-June 16, 2015 and ~16 days (95% CI: 8-32 days) for the period June 17– August 15, 2015. The expected period from the onset of symptoms to death (i.e., the inverse of $p_{I\to D}$ ) was almost constant at ~3.0 days (95% CI: 2.8-3.2 days) for both last periods. The per-contact transmission probability $p_{s\to E}$ values were estimated at ~0.023 (95% CI: 0.02-0.026) in the period April 18-June 16 and ~0.015 (95% CI: 0.01-0.21) in the period June 17– August 15, 2015. Finally, the *Re* obtained through the agent-based simulations dropped to ~1.38

(95% CI: 0.95-1.72) in the period April 18-June 16, 2015 and ~ 0.68 (95% CI: 0.47-1.01) from June 17– August 15, 2015, thus indicating a saturation of the epidemic.

Our analysis succeeded in approximating the actual data for total cases and deaths (*3*). For example, on June 16, 2015 the number of total cases, as reported by the CDC, was 12,990 and the number of deaths was 3,922, while our simulations resulted in 12,963 cases and ~3,940 deaths. On August 14, 2015, the total cases and deaths were 13,485 and 3,952, respectively, and our simulations resulted in 13,437 total cases and 3,993 deaths.

## Contributorship statement

Constantinos Siettos, Lucia Russo,  and Christos Grigoras contributed to the development of the model. Constantinos Siettos and Cleo Anastassopoulou contributed to the data collection, interpretation of the data and drafting the paper. Eleftherios Mylonakis contributed to the interpretation of the data and substantially revised the paper. All authors approved the final manuscript and accepted accountability for all aspects of the work.

## Competing interests

There are no competing interests.

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## Data Sharing Statement

The data used in this study are publicly available from CDC at http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/

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**Table 1.** Key epidemiologic features of the Ebola Virus Disease (EVD) epidemic in Sierra Leone estimated by the model during the first and second study period (December 21, 2014 - April 17, 2015).

| Period | Variable | Mean | 95% CI |
|---|---|---|---|
| **First**<br>(Dec. 21-Feb. 18, 2015) | $p_{rw}$ | 0.37 | 0.33-0.41 |
| | Network density (α) | 0.55 | 0.51-0.58 |
| | Time to death (Days) | 3.6 | 3.3-4.0 |
| | Time to recovery (Days) | 9.5 | 8.6-10.7 |
| | CFR (%) | 32 | 31-33 |
| | $R_e$ | 0.77 | 0.72-0.82 |
| **Second**<br>(Feb. 18-Apr. 17, 2015) | $p_{rw}$ | 0.22 | 0.20-0.24 |
| | Network density (α) | 0.63 | 0.59-0.68 |
| | Time to death (Days) | 3.6 | 3.3-4.0 |
| | Time to recovery (Days) | 8.0 | 6.5-10.5 |
| | CFR (%) | 39 | 38-40 |
| | $R_e$ | 1.98 | 1.33-2.22 |

$p_{rw}$, Rewiring switching probability; CFR, Case fatality rate ($p_{D/I}$); $R_e$, Effective reproductive number

**Table 2.** Outcomes of isolation control policy scenarios on the basis of the expected reproductive number $R_e$, as computed by running the agent-based simulation from April 17 to the mid-June 2015 (keeping fixed all other values of the model parameters). Sparser density refers to a percent reduction of the expected density of the contact network compared to the 0.63 value that was estimated for the second period (February 18 – April 17, 2015).

| **Period** | **% Sparser density** | **Network density** (α) | $R_e$ |
|---|---|---|---|
| (April 18-June 17, 2015) | 10% | ~0.57 | ~1.7 |
| | 20% | ~0.51 | ~1.5 |
| | 30% | ~0.44 | ~1.4 |
| | 40% | ~0.38 | ~1.2 |
| | 50% | ~0.32 | ~1.0 |

**Table 3.** Up-to-date key epidemiologic features of the Ebola Virus Disease (EVD) epidemic in Sierra Leone estimated by the model during the period (June 18- August 15, 2015).

| **Period** | **Variable** | **Mean** | **95% CI** |
|---|---|---|---|
| (June 18- July 16, 2015) | $p_{rw}$ | 0.69 | 0.67-0.72 |
| | Network density (α) | 0.47 | 0.42-0.51 |
| | Time to death (Days) | 3.0 | 2.8-3.2 |
| | Time to recovery (Days) | 20 | 16-30 |
| | CFR (%) | 10 | 8-12 |
| | $R_e$ | 1.38 | 0.95-1.72 |
| (July 16- August 15, 2015) | $p_{rw}$ | 0.75 | 0.69-0.80 |
| | Network density (α) | 0.46 | 0.37-0.53 |
| | Time to death (Days) | 3.0 | 2.8-3.2 |
| | Time to recovery (Days) | 16 | 8-32 |
| | CFR (%) | 10 | 8-12 |
| | $R_e$ | 0.68 | 0.47-1.01 |

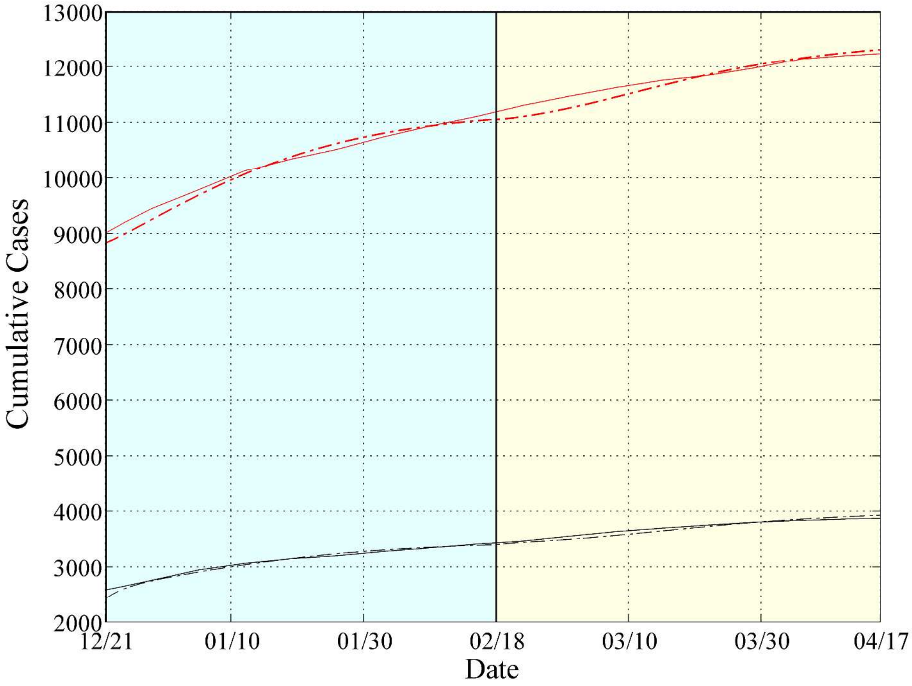
$p_{rw}$, Rewiring switching probability; CFR, Case fatality rate ($p_{D/I}$); $R_e$, Effective reproductive number

# FIGURE LEGENDS

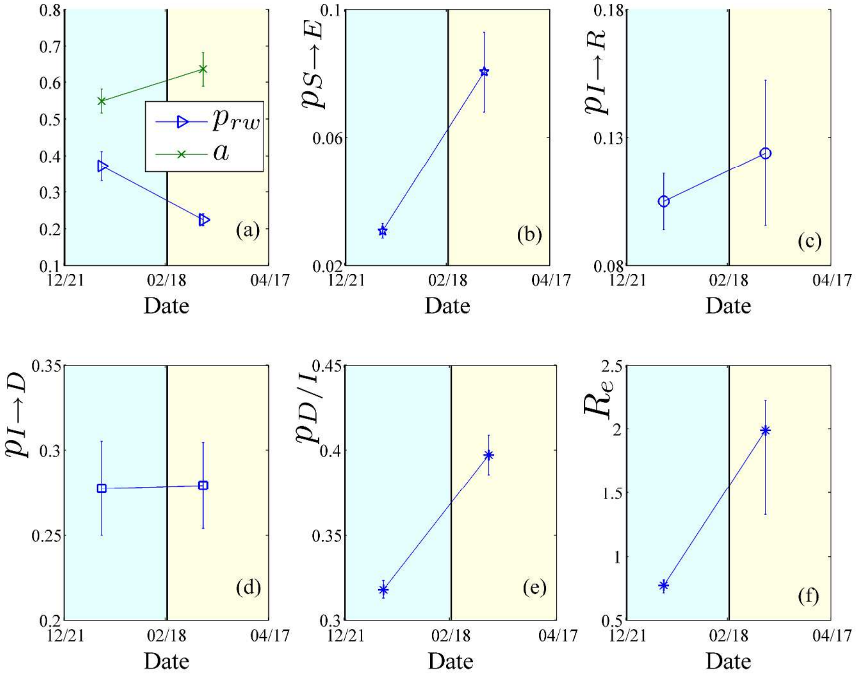
**Figure 1. Simulation Results for Sierra Leone from December 21, 2014 to April 17, 2015.** Expected cumulative cases of infected (dotted red) and dead (dotted black). WHO data are depicted by solid lines. The period under study has been tessellated into two windows with a length of 60 days each. For each window, the model parameters are estimated based on the data reported from WHO.

**Figure 2. Estimated model parameters for Sierra Leone from December 21, 2014 to April 17, 2015. (a)** Evolution of contact network characteristics: switching probability ($p_{rw}$) and density ratio of the transmission network ($a$). **(b)** Per-contact transmission probability ($p_{s\rightarrow E}$). **(c)** 1/{recovery period} ($p_{I\rightarrow R}$). **(d)** 1/{period from inset of symptoms to death} ($p_{I\rightarrow D}$). **(e)** Case fatality rate ($p_{D/I}$). **(f)** Effective reproductive number ($R_e$). 95% Confidence intervals are also shown.

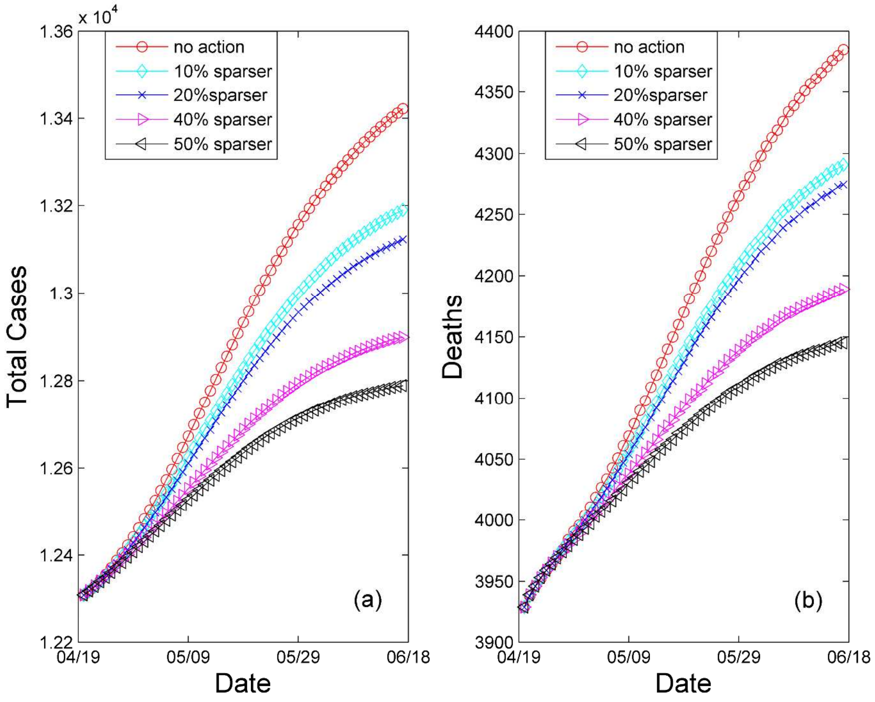
**Figure 3. Forecasting of the evolution of the epidemic from April 18 to June 17, 2015 under different control scenarios**. Network density values were compared to the density of the social network estimated for the period February 18-April 17, 2015. **(a)** Total Cases, **(b)** Deaths. The "no further action" scenario is also depicted.



Simulation Results for Sierra Leone from December 21, 2014 to April 17, 2015. Expected cumulative cases of infected (dotted red) and dead (dotted black). WHO data are depicted by solid lines. The period under study has been tessellated into two windows with a length of 60 days each. For each window, the model parameters are estimated based on the data reported from WHO.



Estimated model parameters for Sierra Leone from December 21, 2014 to April 17, 2015. (a) Evolution of contact network characteristics: switching probability and density ratio of the transmission network. (b) Per-contact transmission probability. (c) 1/{recovery period}. (d) 1/{period from inset of symptoms to death}. (e) Case fatality rate. (f) Effective reproductive number. 95% Confidence intervals are also shown.



Forecasting of the evolution of the epidemic from April 18 to June 17, 2015 under different control scenarios. Network density values were compared to the density of the social network estimated for the period February 18-April 17, 2015. (a) Total Cases, (b) Deaths. The "no further action" scenario is also depicted.

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# Title Page

# Forecasting and Control Policy Assessment for the Ebola Virus Disease (EVD) Epidemic in Sierra Leone Using Small-World Networked Model Simulations

Constantinos I. Siettos[1], Cleo Anastassopoulou[2], Lucia Russo[3], Christos Grigoras[1,4], Eleftherios Mylonakis[4]

**Authors' affiliations:**
[1] School of Applied Mathematics and Physical Sciences, National Technical University of Athens, Athens, Greece.
[2] Division of Genetics, Cell and Developmental Biology, Department of Biology, University of Patras, Patras, Greece.
[3] Consiglio Nazionale di Ricerca, Napoli, Italy.
[4] Division of Infectious Diseases, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI, USA.

**Corresponding author:**

Constantinos I. Siettos: Associate Professor Computational Science & Engineering, School of Applied Mathematics and Physical Sciences, National Technical University of Athens, 9, Heroon Polytechniou Str., GR-157 80 Athens, Greece. Tel.: +30 210-772-3950; E-mail: ksiet@mail.ntua.gr

Eleftherios Mylonakis, M.D., Ph.D., FIDSA, Dean's Professor of Medical Science (Medicine, and Molecular Microbiology and Immunology), Chief, Infectious Diseases Division, Warren Alpert Medical School of Brown University, Rhode Island Hospital 593 Eddy Street, POB, 3rd Floor, Suite 328/330, Providence, RI 02903, Tel: 401-444-7856 / Fax: 401-444-8179.

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## Abstract

**Objectives:** As the Ebola Virus Disease (EVD) is still sustained in Sierra Leone, we analyzed the epidemic for the latest period (December 21, 2014 -April 17, 2015) using a small-world networked model and forecasted its evolution. Policy-control scenarios for the containment of the epidemic were also examined.

**Methods:** We developed an agent-based model with 6 million individuals (the population of Sierra Leone) interacting through a small-world social network. The model incorporates the main epidemiologic factors, including the effect of burial practices to virus transmission. The effective reproductive number (*Re)* was evaluated directly from the agent-based simulations. Estimates of the epidemiologic variables were computed on the basis of the official cases as reported by the Centers for Disease Control and Prevention (CDC).

**Results:** From December 21, 2014 to February 18, 2015 the epidemic was in recession compared to previous months, as indicated by the estimated effective reproductive number (*Re*) of ~0.77 (95% CI: 0.72-0.82). From February 18 to April 17, 2015, *Re* rose above criticality (~1.98, 95% CI: 1.33-2.22), flashing a note of caution for the situation. By projecting in time, we predicted that the epidemic would continue through July 2015. Our predictions were close to the cases reported by CDC by the end of June, verifying the criticality of the situation. In light of these developments, while revising our manuscript, we expanded our analysis to include the most recent data (until August 15, 2015). By mid-August, *Re* has fallen below criticality and the epidemic is expected to fade out by early December 2015.

**Conclusions:** Our results call for the continuation of drastic control measures, which in the absence of an effective vaccine or therapy at present can only translate to isolation of the infected section of the population, to contain the epidemic.

**Keywords:** EBOV, Sierra Leone, Effective reproductive number, Forecasting, Communicable Disease Control, Agent-Based Modeling, Social Transmission Network

## Article summary

### Strengths and limitations of this study

- The greatest strength of this study stems from the undertaken mathematical approach of choice, integrating agent-based modeling on complex networks and the so-called Equation-Free approach.
- Various important epidemiologic parameters were assessed and accurate short-term forecasts of the evolution of the Ebola Virus Disease (EVD) epidemic in Sierra Leone were obtained.
- Another advantage of the proposed methodology is that it allows for the rapid evaluation of different policy-control scenarios that could lead to the containment of the epidemic.
- Our predictions were verified by the official case count reported by CDC.
- The most important limitation of our study pertains to the quality and accuracy of the outbreak data that were “fed” to the mathematical model compared to the real figures.
- Even though underreporting of cases and deaths is to be expected under the particular circumstances of such a severe epidemic, real-life figures agree well with the projections of our analysis.

## Introduction

The worst Ebola Virus Disease (EVD) epidemic in history continues to ravage West Africa. The epidemic began with the report of 49 cases and 29 deaths in Guinea on March 22, 2014 (*1*). Liberia reported its first laboratory-confirmed cases on March 30, 2014, while the first cases in Sierra Leone were reported on May 28, 2014 (*2*). Following regular daily population movements for trade and family visitation, the virus crossed the local porous international borders, establishing chains of transmission not just in small villages, where it would have been easier to contain it, but also in large urban centers. Insufficient public health infrastructure, poor sanitation conditions, lack of education about the disease and unsafe traditional burial practices have also contributed to the spread of the epidemic in the region (*2*).

In Liberia, one of the most affected countries, as of April 20, 2015, a total of 10,042 cases have been recorded, while the toll of death has exceeded 4,480 (*3*). In early March a halt of the epidemic was announced, and even though a new case was confirmed on March 20, 2015, the epidemic is considered to have ceased, while the situation in Sierra Leone is notably different. With more than 12,360 cases and 3,900 deaths until now, Sierra Leone experienced a drop in new cases in January 2015 and authorities loosened mobilization restriction measures to support economic activity (*4*). However, recent World Health Organization WHO updates on the status of the EVD epidemic in this West African nation report a flare up (*3*), with a significant increase among the community of fishermen living in the coastal area of Aberdeen in Freetown (*5*). The synchronous occurrence of over 20 cases suggested they had been infected by a single source, possibly an unsafe burial (*5*).

In light of these recent developments, we analyzed the EVD epidemic dynamics in Sierra Leone for the period between December 21, 2014 and April 17, 2015, using an agent-based, social network model that we reported recently and that proved to provide accurate predictions for the case of Liberia (*6*). For this purpose, the latest official case counts from WHO were fitted to the model, following the so-called Equation-Free approach (*7*). Our main objective was to obtain estimates of key epidemiologic parameters, such as the indicative of secondary infections effective reproductive number (*Re*), the case fatality rate, the per-contact transmission probability and the mean time from symptoms onset to recovery or to death, in order to study the evolving dynamics through the social transmission network whose structure and density are also examined. Secondary objectives of the study included the exploration of different policy-control scenarios that could lead to reduced *Re* values, and, thereby, to the containment of the epidemic.

## Methods

We developed an agent-based model for the study of the Ebola epidemic (*6*) with $N$ individuals that interact through a Watts & Strogatz (WS) (*8*) small-world network that approximates some attributes of the real social interactions, which are characterized by relatively high clustering and short social distances between them. Here, the network was constructed with the Newman-Watts (*9*) algorithm, in which short-cut edges are added between pairs of nodes with a probability, in the same way as in a WS network, but without removing edges from the underlying lattice. The algorithm starts with a one-dimensional ring network with $k$ local-nearest neighbors per node and with a probability $p_{rw}$ that a link is added between two nodes. Hence, the mean number of additional shortcuts is $p_{rw}\, k\, N$, and the mean total degree of the network is $2\, k\, N\,(1+ p_{rw})$. In the constructed small-world network we can adjust the density of the network, say $\alpha$, at will, by randomly adding or subtracting the required number of links.

Agents are categorized in five discrete states: *Susceptible* $(S)$, *Exposed* $(E)$, *Infected* $(I)$, *Dead of the disease but not yet buried* $(D_I)$, *Dead of the disease and safely buried* $(D_b)$, and *Recovered* $(R)$ (*6*). The $D_I$ infectious state includes agents who die, but whose burial entails risk for onward virus transmission. The transition between states is modeled as a discrete-time, discrete state *non-Markov random process*. Within this framework, the state space over the set of the network links is represented by $Y(\mathbf{V})$, where $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$ is the set of the states of individual $v_k$.

The agent-based rules that govern the dynamics of the epidemic on a daily basis read as follows:

$$p\left(Y_{v_k}(t+1) = D_b \mid Y_{v_k}(t-1) = D_I\right) = 1 \tag{1}$$

$$p\left(Y_{v_k}(t+1) = E \mid Y_{v_l}(t) = I, Y_{v_l}(t) = D_I \right) = p_{S\to E}\,,\ v_l \in \Re_{v_k} \tag{2}$$

$$p\left(Y_{v_k}(t+1) = I \mid Y_{v_k}(t) = E\right) = p_{E\to I} \tag{3}$$

$$p\left(Y_{v_k}(t+1) = D_I \mid Y_{v_k}(t) = I\right) = p_{I\to D} \tag{4}$$

$$p\left(Y_{v_k}\left(t+1\right)=R \mid Y_{v_k}\left(t\right)=I\right)=p_{I\rightarrow R} \quad (5)$$

where $p_{S\rightarrow E}$ is the per infected contact transmission probability (still alive or dead, but not yet buried), $p_{E\rightarrow I}$, is the inverse of the incubation period, $p_{I\rightarrow D}$ is the inverse of the time from symptoms onset to death, $p_{I\rightarrow R}$ is the inverse of the recovery period, and, $p_{D/I}$, is the ratio of deaths to the infected population (*6*). The rate of the incubation period is taken to be constant, set at $p_{E\rightarrow I}=\frac{1}{9}$, as reported by the Who Ebola Response Team (*10*). $\Re_{v_k}$ denotes the neighborhood of an individual $v_k$. This first rule sets the time period from death to burial to two days, during which family members and loved ones may be infected due to physical contact with the dead, still-contagious body. Long-range links of a dead, yet potentially infectious, agent are cut, reflecting the fact that only relatives and close community members can be infected during unsafe funeral practices and rites. The second rule implies that a susceptible agent gets exposed to the disease with a rate determined by the probability $p_{S\rightarrow E}$ per infected contact (still alive or dead, but not yet buried). The third rule implies that an exposed agent becomes infectious with a rate determined by the probability $p_{E\rightarrow I}$, whose inverse corresponds to the incubation period, i.e. the time from exposure to symptoms onset. Rules (4) and (5) define the case fatality rate, $p_{D/I}$: an agent dies of the disease with a rate determined by the probability $p_{I\rightarrow D}$ (whose inverse is the time from symptoms onset to death) (Rule (4)); alternatively, an agent could recover with a rate determined by the probability $p_{I\rightarrow R}$ (Rule (5)).

The effective reproductive ratio $R_e$, defined as the average number of secondary infections produced by a typical infective person, is also computed directly from the agent-based simulations.

Based on the demographics reported by the United Nations (UN), the population of Sierra Leone is 6 million (*11*). Time series of the official Ebola case counts from the Centers for Disease Control and Prevention (CDC) were used for model fitting (*3*). These case counts were collected from public data released by the World Health Organization (WHO) (*12*) and CDC (3). Even though these data sets do not distinguish between suspect, probable and laboratory-confirmed case counts, they are considered to represent the best available estimates of the current state of the epidemic in the severely afflicted West African countries.

Case data, which included cumulative incidence and cumulative deaths by date of report for Sierra Leone, were retrieved on April 24, 2015.

Simulations were performed using December 21, 2014 as an initial date and a time horizon of 60 days with an equal sliding window time interval; the last date was April 17, 2015. Thus, fitted values of the network and model parameters, as well as estimates of the effective reproductive ratio, were computed in sequences of succeeded time intervals of 60 days corresponding to 2 periods (December 21, 2014 – February 18, 2015 and February 18, 2015 – April 17, 2015). The initial conditions for the starting date of December 21, 2014 were calculated on the basis of agent-based simulations from May 27, 2014, i.e. the date on which the first cases were officially reported from WHO (*2*), following the procedure described in detail elsewhere (*6*). In particular, we obtained the following (expected) numbers for December 21, 2014: $E_0 = 450$, $I_0 = 901$, $D_{b0} = 2390$, $D_{I0} = 28$, $R_0 = 5579$; the estimated cumulative number of cases then was 8,828.

The expected (averaged) values of the agents' states $Y(v_k) \equiv Y_{v_k} = \{S, E, I, D_b, D_I, R\}$ were computed over $N_r = 8$ network realizations and $N_s = 100$ simulations for each one of the network realizations. The model parameters were fitted to the reported data using a trust-region-reflective approach for nonlinear minimization, implemented for parameter estimation (*13*) exploiting the Equation-Free approach (*7,14-18*). Matlab (*19*) was the simulation environment of choice, while the model was programmed in Fortran 90 and linked to Matlab through mex files.

To forecast the evolution of the Ebola virus epidemic in Sierra Leone, we used the values of the model parameters as estimated in the last period; the resulting parameter values were then fed to the simulator using as coarse initial conditions the values of $\{S, E, I, D_b, D_I, R\}$ as computed on April 17, 2015. We tested the effect of control policy scenarios by reducing the density of the network structure as estimated in the second period. Sparser network densities could reflect partial isolation of the population, restriction of social mobilization combined with an expanded public campaign for increased awareness.

## Results and Discussion

The cumulative numbers of infected and dead obtained by the model compared to the reported cases in Sierra Leone are shown in Figure 1. Our framework succeeds in approximating the actual data for total cases and deaths (*3*). For example, on December 21, 2014 the number of total cases, as reported by the WHO, was 9,004 and the number of deaths was 2,582, while our simulations resulted in 8,828 cases and ~2,400 deaths. On February 18, 2015, the total cases and deaths were 11,103 and 3,408, respectively, and our simulations resulted in 11,049 total cases and 3,394 deaths. Finally, on April 17, 2015, the reported total cases and deaths were 12,244 and 3,865, respectively; our simulations resulted in 12,299 total cases and 3,919 deaths.

The epidemiologic parameters that were obtained through the optimization approach are illustrated in Figure 2 and a summary of the estimated epidemic parameters for the period under study, together with their 95% confidence intervals, is presented in Table 1. Panel (a) depicts the evolution of the estimated network characteristics, $p_{rw}$ and $a$, while panels (b-e) illustrate the model parameters $p_{S\to E}$, $p_{D/I}$, $p_{I\to R}$ and $p_{I\to D}$ that fit best to the reported EVD epidemic dynamics in the country. The evolution of the estimated effective reproductive number $R_e$ in Sierra Leone is shown in panel (f).

More specifically, the contact network of Sierra Leone exhibits a rather random structure with a rewiring switching probability ( $p_{rw}$ ) of ~0.37 (95% CI: ~0.33-0.41) that falls down to ~0.22 (95% CI: 0.20-0.24) during the study period (Figure 2a). A slight increase is shown in the density ratio of the network as represented by $a$, which was ~0.54 (95% CI: ~0.51-0.58) during the first period (December 21, 2014 – February 18, 2015) and ~0.63 (95% CI: 0.59-0.68) during the second period of the study (February 18, 2015 – April 17, 2015) (Figure 2a). The differences of the network characteristics between the two periods indicate a more clustered, yet denser contact network during the second period that could partially reflect a relaxation of awareness in the first period, when the epidemic seemed to decline. The per-contact transmission probability $p_{S\to E}$ values were estimated at ~0.03 (95% CI: 0.028-0.033) in the first period and ~0.08 (95% CI: 0.067-0.09) in the second period (Figure 2b). The expected period from the onset of symptoms to recovery (i.e., the inverse of $p_{I\to R}$) was ~9.5 days (95% CI: 8.6-10.7 days) during the first period and ~8 days (95% CI: 6.5-10.5 days) for the second period of study (Figure 2c). The expected time interval from the onset of symptoms to death (i.e., the inverse of $p_{I\to D}$) was constant at ~3.6 days (95% CI: 3.3-4.0 days) during the period of study (Figure 2d). The case fatality rate ( $p_{D/I}$ ) that was estimated to be ~32% (95% CI: 31-33%) for the period extending from late December 2014 to February 18 2015, increased to ~39% (95% CI: 38-40%) from February 18 to April 17 (Figure 2e). Finally, the effective reproductive number $R_e$, as computed using the agent-based simulator, was ~0.77 (95% CI: 0.72-0.82) from December 21, 2014 to February 18, 2015, rising up to ~1.98 (95% 1.33-2.22) from February18, 2015 to April 17, 2015 (Figure 2f).

Regarding the epidemic parameters, our estimates are quite close to the ones reported by the WHO Ebola Response Team and other groups. For example, Ansumana *et al*. (*20*) reported a 31% CFR at Hastings center, while the National Institute of Communicable diseases (NICD) reports a CFR of 32% for Sierra Leone on April 5, 2015 (*21*); a mean of 31.6% CFR was reported for Sierra Leone from the WHO Ebola response team as of September 14, 2014 (*10*). Gomes *et al*. (*22*) reported an ~8 day-period from the onset of symptoms to recovery, while in a recent study by the WHO Ebola response team (*23*) a period of 10.6 days (with a SD of 8.2 days) was reported from symptoms onset to hospital discharge for individuals of older than 45 years old. In the same paper, a period of ~6 days (with equal SD) is reported from symptoms onset to death for the same age group. The same delay period from symptoms onset to death was also reported in Ansumana *et al*. (*20*).

Simulations show that the expected cumulative number of infected cases may reach as high as 13,400 by June 17, while the cumulative number of dead may exceed 4,300, if no further action is undertaken. Hence, we decided to perform an assessment of the impact of potential control strategies. Based on the recently announced isolation policy (*24*), we simulated the influence on the epidemic dynamics of sparser, with respect to the estimated network density of the second period, network densities, by 10%, 20%, 30%, 40% and 50%. We tested these scenarios by reducing analogously the expected density of the contact network as estimated during the second period and running the agent-based simulation from April 18 until June17, 2015, keeping all other values of the model parameters fixed.

The results of the exploration of these different scenarios are summarized in Table 2 and portrayed graphically in Figure 3. The “no further action” case, with respect to the estimated current network structure is also depicted in Figure 3 for comparison. By applying a 10% reduction in the network density (yielding an $a$ of ~0.57), the expected reproductive number $R_e$ was estimated to be ~1.7. Accordingly, for a 20% reduction in the network density (yielding an $a$ of ~0.51), $R_e$ was estimated to be ~1.51. Reductions of 30%, 40% and 50% yielding network densities of ~0.44, ~0.38 and ~0.32 respectively, resulted in $R_e$ values of

~1.42, ~1.23 and ~1.05 correspondingly (Table 2). As shown, even large reductions in the density of the network will not lower the $R_e$ below unity soon.

A study by Khan *et al*. that obtained robust estimates for the basic reproductive ratio $R_0$ in both Liberia and Sierra Leone showed that effective isolation is required to bring the value of $R_0$ to less than 1, and hence control the outbreak (*25*). Khan *et al*. suggested that the contact rate in isolation should be less than one quarter of that for the infected non-isolated population, and that, the fraction of high-risk individuals should be brought to less than 10% of the overall susceptible population, to halt the epidemic (*25*).

In reality, the reduction in the network density could potentially reflect analogous reductions in social interactions further to the current restrictions of community mobilization. Examples would include raising public awareness and/or strengthening medical care. The country's National Ebola Response Centre has already announced a 3-day lockdown that will affect around 2.5 million people (*20*). Nevertheless, it is worth noticing that even with a 30% reduction in the social network density, the epidemic shows no signs of fading out until June 17 and we estimate that new cases will continue to be recorded.

In conclusion, we found that the EVD epidemic in Sierra Leone was in recession in the period between December 21, 2014 through mid-February, 2015, as reflected by the <1 value of the reproductive number for this period. However, during the second study period (i.e., from February 18 to April 17, 2015), the epidemic has spiked and the reproductive number was estimated to be well above criticality, with the potential to persist at this level beyond the end of June and through July. Control measures associated with mobilization restrictions were also evaluated. Our findings, supported by real epidemiologic data and the projection of a spilling over of the epidemic to mid-June, indicate that the measures implemented so far are inadequate. Taken in their totality, these findings indicate that the epidemic, even with strict control isolation policies in effect, will go on through July with a probability of fading out thereafter if policies are implemented and consistently kept in place. Immediate, more intense efforts are needed before further complications emerge. Reducing the effective density of the derived contact small-world-like network, through limited social interactions, has the potential to improve the current situation. Our results and predictions were verified from the official data reported by CDC for the corresponding period of study. Hence, our approach seems promising to forecast re-emergent outbreaks in other vulnerable regions of Africa, such as Eastern and Central Africa, where Ebola outbreaks have traditionally occurred in the past. Estimations through clinical studies of important factors such as the contact transmission probability, mortality and recovery rate, incubation periods as well as detailed age-specific data as the epidemic develops in space and time, would enhance our ability to better model, forecast and design efficient control policies.

However, the usefulness of mathematical models should not be overestimated. Despite the significant technological progress and concentrated wealth, breakdowns and cuts in public health infrastructures worldwide are (the) major reasons for boosting epidemics. Liberia and Sierra Leone, the two countries that have been worst affected from the Ebola epidemic had an almost non-existent health care system: as reported Liberia with a population of more than 4 million people had just 51 physicians and Sierra Leone with a population exceeding 6 million had just 136 physicians (26).

### *Update to the case of Sierra Leone (period April 18-August 15, 2015)*

Since the results we obtained by analyzing the reported data until April 17, 2015 showed that the epidemic was sustained in Sierra Leone, we decided to investigate further the current trends of the epidemic dynamics. Therefore, we expanded our analysis by taking into account the reported data for the country for the very last period (April 18-August 15, 2015). The results of this expanded analysis indicate a declining trend in the transmission potential of the virus, as shown in Table 3. More specifically, ( $p_{rw}$ ) rose significantly in the period April 18-June 16, 2015 to ~0.69 (95% CI: ~0.67-0.72) with a further slight increase in the very last period (June 17-August 15, 2015) to ~0.75 (95% CI: 0.69-0.80). The density ratio of the network as represented by $a$ , did not show significant changes: in the period April 18-June 16, 2015 it was found to be ~0.47 (95% CI: ~0.42-0.51) and ~0.46 (95% CI: 0.37-0.53) during the period June 17-August 15, 2015. The case fatality rate ( $p_{D|I}$ ) dropped to ~10% (95% CI: 8-12%) for both last periods. The expected period from the onset of symptoms to recovery (i.e., the inverse of $p_{I\to R}$ ) was ~20 days (95% CI: 16-30 days) during the period April 18-June 16, 2015 and ~16 days (95% CI: 8-32 days) for the period June 17– August 15, 2015. The expected period from the onset of symptoms to death (i.e., the inverse of $p_{I\to D}$ ) was almost constant at ~3.0 days (95% CI: 2.8-3.2 days) for both last periods. The per-contact transmission probability $p_{s\to E}$ values were estimated at ~0.023 (95% CI: 0.02-0.026) in the period April 18-June 16 and ~0.015 (95% CI: 0.01-0.21) in the period June 17– August 15, 2015. Finally, the *Re* obtained through the agent-based simulations dropped to ~1.38 (95% CI: 0.95-1.72) in the period April 18-June 16, 2015 and ~ 0.68 (95% CI: 0.47-1.01) from June 17– August 15, 2015, thus indicating a saturation of the epidemic.

Our analysis succeeded in approximating the actual data for total cases and deaths (*3*). For example, on June 16, 2015 the number of total cases, as reported by the CDC, was 12,990 and the number of deaths was 3,922, while our simulations resulted in 12,963 cases and ~3,940 deaths. On August 14, 2015, the total cases and deaths were 13,485 and 3,952, respectively, and our simulations resulted in 13,437 total cases and 3,993 deaths.

## Contributorship statement

Constantinos Siettos, Lucia Russo, and Christos Grigoras contributed to the development of the model. Constantinos Siettos and Cleo Anastassopoulou contributed to the data collection, interpretation of the data and drafting the paper. Eleftherios Mylonakis contributed to the interpretation of the data and substantially revised the paper. All authors approved the final manuscript and accepted accountability for all aspects of the work.

## Competing interests

There are no competing interests.

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## Data Sharing Statement

No additional data available.

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**Table 1.** Key epidemiologic features of the Ebola Virus Disease (EVD) epidemic in Sierra Leone estimated by the model during the first and second study period (December 21, 2014 - April 17, 2015).

| Period | Variable | Mean | 95% CI |
|---|---|---|---|
| **First**<br>(Dec. 21-Feb. 18, 2015) | $p_{rw}$ | 0.37 | 0.33-0.41 |
| | Network density (α) | 0.55 | 0.51-0.58 |
| | Time to death (Days) | 3.6 | 3.3-4.0 |
| | Time to recovery (Days) | 9.5 | 8.6-10.7 |
| | CFR (%) | 32 | 31-33 |
| | $R_e$ | 0.77 | 0.72-0.82 |
| **Second**<br>(Feb. 18-Apr. 17, 2015) | $p_{rw}$ | 0.22 | 0.20-0.24 |
| | Network density (α) | 0.63 | 0.59-0.68 |
| | Time to death (Days) | 3.6 | 3.3-4.0 |
| | Time to recovery (Days) | 8.0 | 6.5-10.5 |
| | CFR (%) | 39 | 38-40 |
| | $R_e$ | 1.98 | 1.33-2.22 |

$p_{rw}$, Rewiring switching probability; CFR, Case fatality rate ($p_{D/I}$); $R_e$, Effective reproductive number

**Table 2.** Outcomes of isolation control policy scenarios on the basis of the expected reproductive number $R_e$, as computed by running the agent-based simulation from April 17 to the mid-June 2015 (keeping fixed all other values of the model parameters). Sparser density refers to a percent reduction of the expected density of the contact network compared to the 0.63 value that was estimated for the second period (February 18 – April 17, 2015).

| **Period** | **% Sparser density** | **Network density** (α) | $R_e$ |
|---|---|---|---|
| (April 18-<br>June 17,<br>2015) | 10% | ~0.57 | ~1.7 |
| | 20% | ~0.51 | ~1.5 |
| | 30% | ~0.44 | ~1.4 |
| | 40% | ~0.38 | ~1.2 |
| | 50% | ~0.32 | ~1.0 |

**Table 3.** Up-to-date key epidemiologic features of the Ebola Virus Disease (EVD) epidemic in Sierra Leone estimated by the model during the period (June 18- August 15, 2015).

| Period | Variable | Mean | 95% CI |
|---|---|---|---|
| (June 18- July 16, 2015) | $p_{rw}$ | 0.69 | 0.67-0.72 |
| | Network density (α) | 0.47 | 0.42-0.51 |
| | Time to death (Days) | 3.0 | 2.8-3.2 |
| | Time to recovery (Days) | 20 | 16-30 |
| | CFR (%) | 10 | 8-12 |
| | $R_e$ | 1.38 | 0.95-1.72 |
| (July 16- August 15, 2015) | $p_{rw}$ | 0.75 | 0.69-0.80 |
| | Network density (α) | 0.46 | 0.37-0.53 |
| | Time to death (Days) | 3.0 | 2.8-3.2 |
| | Time to recovery (Days) | 16 | 8-32 |
| | CFR (%) | 10 | 8-12 |
| | $R_e$ | 0.68 | 0.47-1.01 |

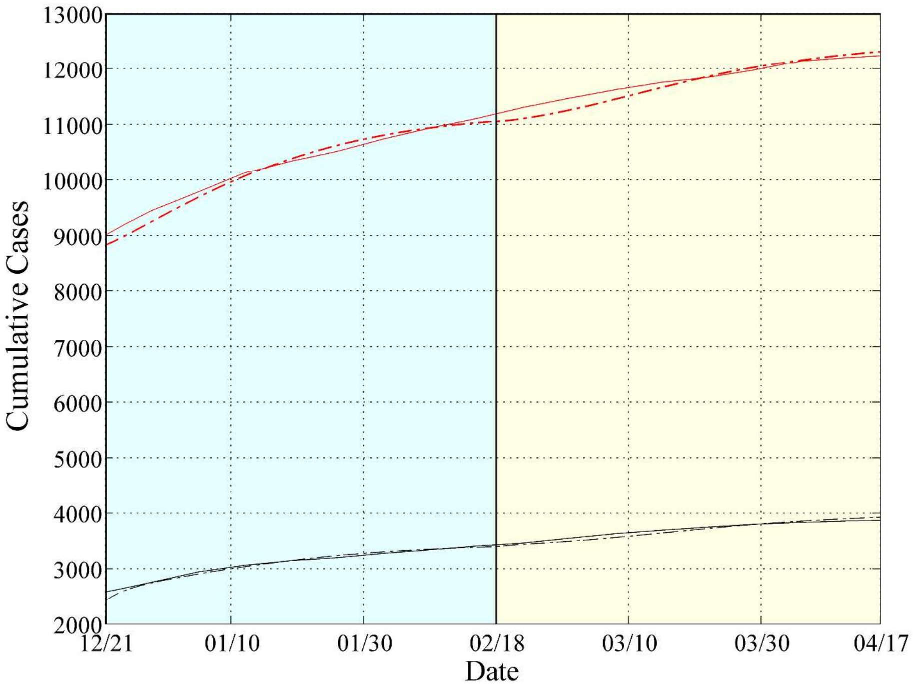
$p_{rw}$, Rewiring switching probability; CFR, Case fatality rate ($p_{D/I}$); $R_e$, Effective reproductive number

## FIGURE LEGENDS

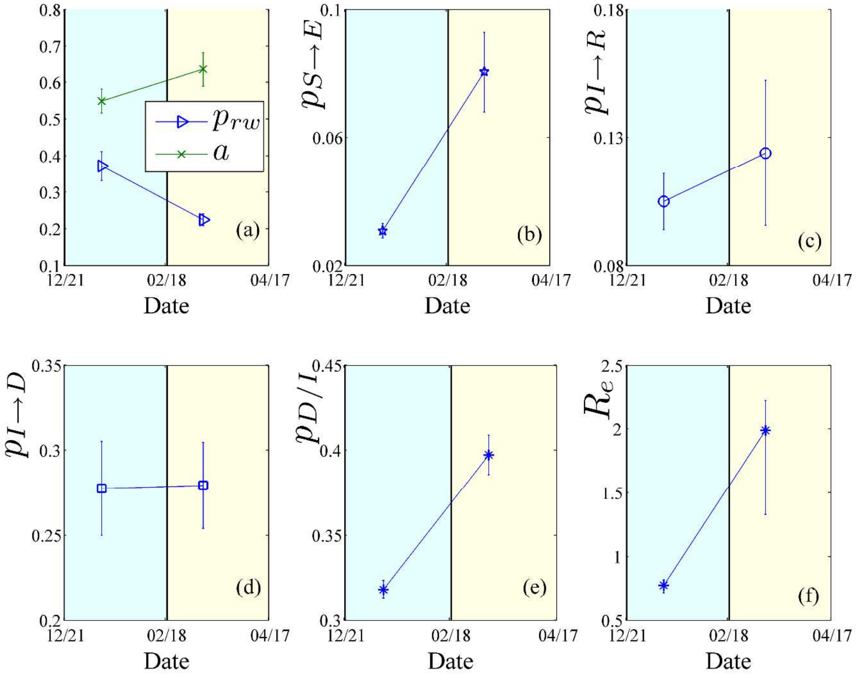
**Figure 1. Simulation Results for Sierra Leone from December 21, 2014 to April 17, 2015.** Expected cumulative cases of infected (dotted red) and dead (dotted black). WHO data are depicted by solid lines. The period under study has been tessellated into two windows with a length of 60 days each. For each window, the model parameters are estimated based on the data reported from WHO.

**Figure 2. Estimated model parameters for Sierra Leone from December 21, 2014 to April 17, 2015. (a)** Evolution of contact network characteristics: switching probability ( $p_{rw}$ ) and density ratio of the transmission network ( $a$ ). **(b)** Per-contact transmission probability ( $p_{s\rightarrow E}$ ). **(c)** 1/{recovery period} ( $p_{I\rightarrow R}$ ). **(d)** 1/{period from inset of symptoms to death} ( $p_{I\rightarrow D}$ ). **(e)** Case fatality rate ( $p_{D/I}$ ). **(f)** Effective reproductive number ( $R_e$ ). 95% Confidence intervals are also shown.

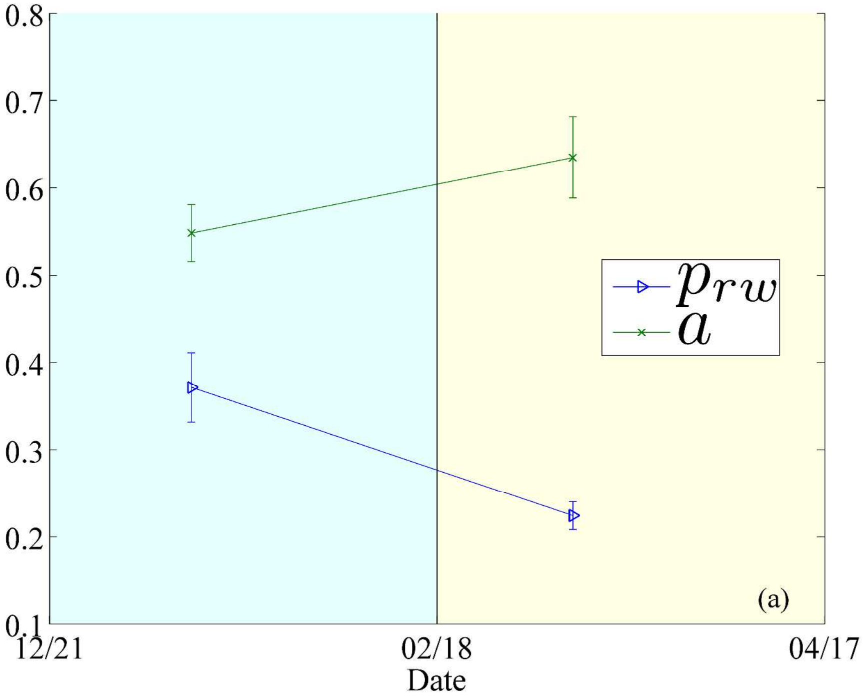
**Figure 3. Forecasting of the evolution of the epidemic from April 18 to June 17, 2015 under different control scenarios**. Network density values were compared to the density of the social network estimated for the period February 18-April 17, 2015. **(a)** Total Cases, **(b)** Deaths. The "no further action" scenario is also depicted.

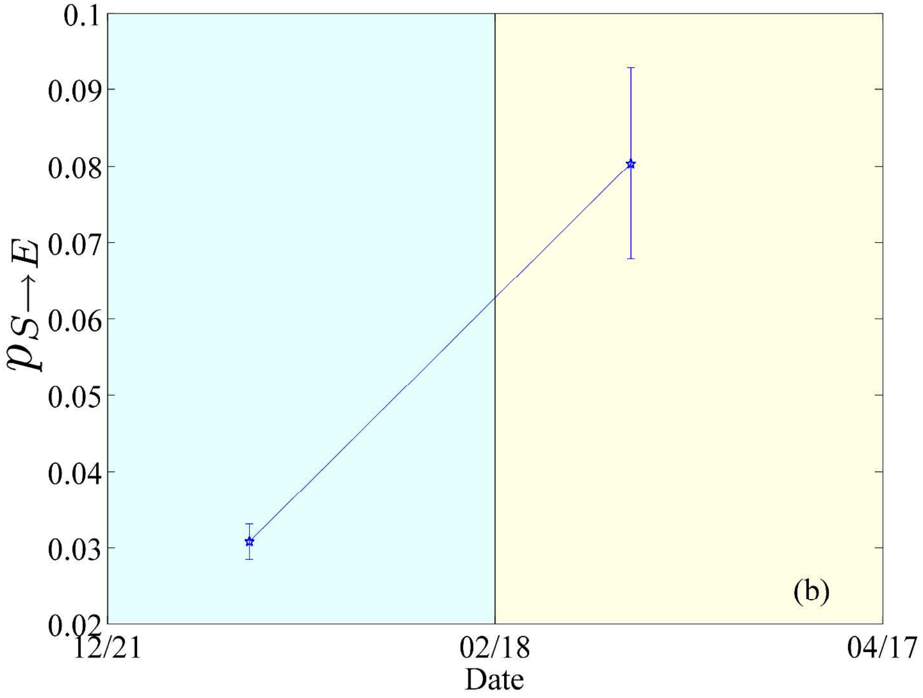


Simulation Results for Sierra Leone from December 21, 2014 to April 17, 2015. Expected cumulative cases of infected (dotted red) and dead (dotted black). WHO data are depicted by solid lines. The period under study has been tessellated into two windows with a length of 60 days each. For each window, the model parameters are estimated based on the data reported from WHO.

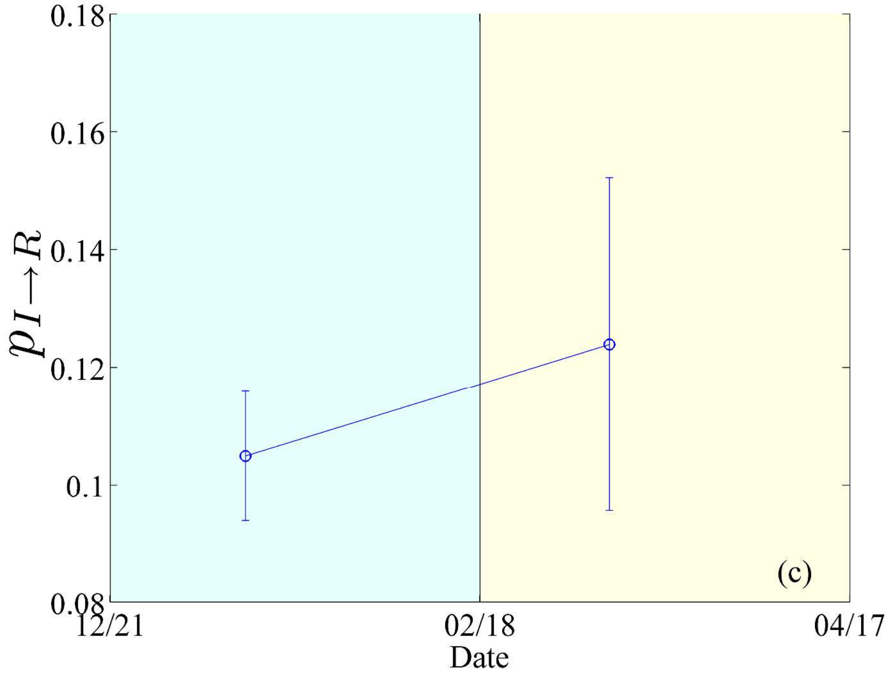


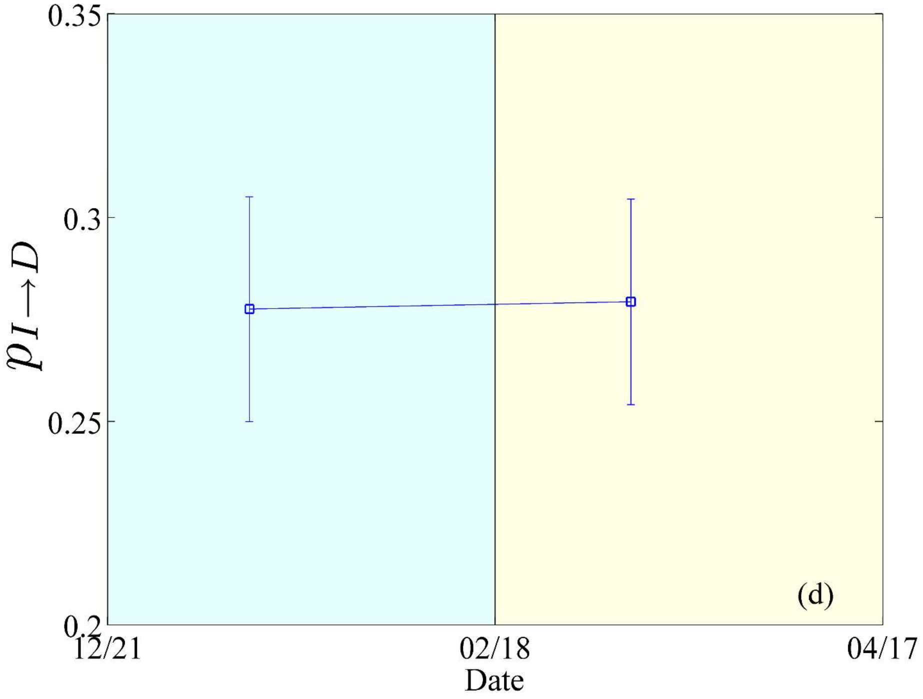
Estimated model parameters for Sierra Leone from December 21, 2014 to April 17, 2015. (a) Evolution of contact network characteristics: switching probability and density ratio of the transmission network. (b) Per-contact transmission probability. (c) 1/{recovery period}. (d) 1/{period from inset of symptoms to death}. (e) Case fatality rate. (f) Effective reproductive number. 95% Confidence intervals are also shown.

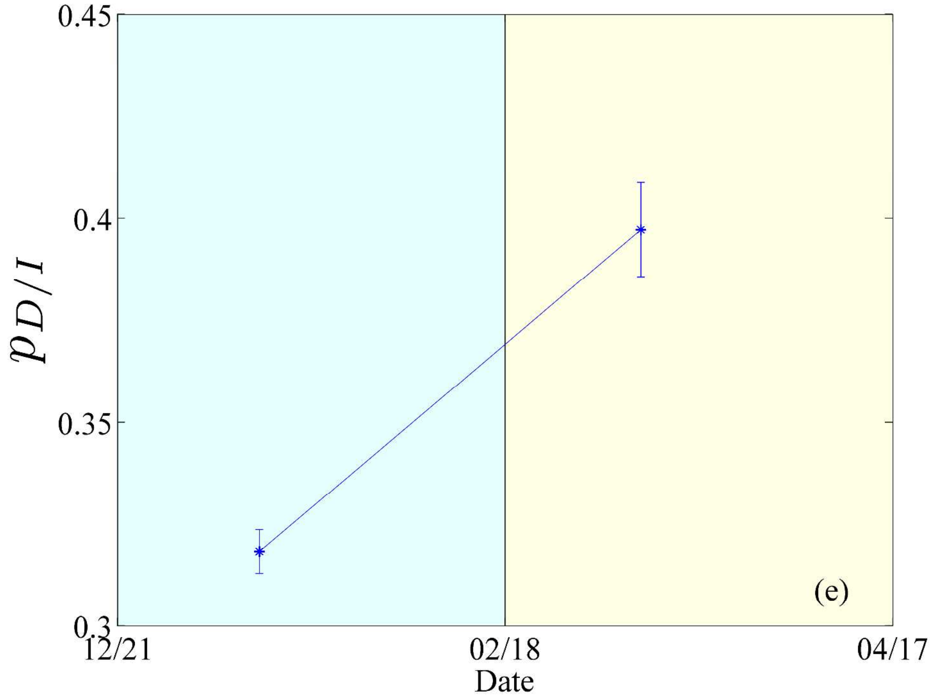

0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
12/21
02/18
04/17
Date
$p_{rw}$
$a$
(a)

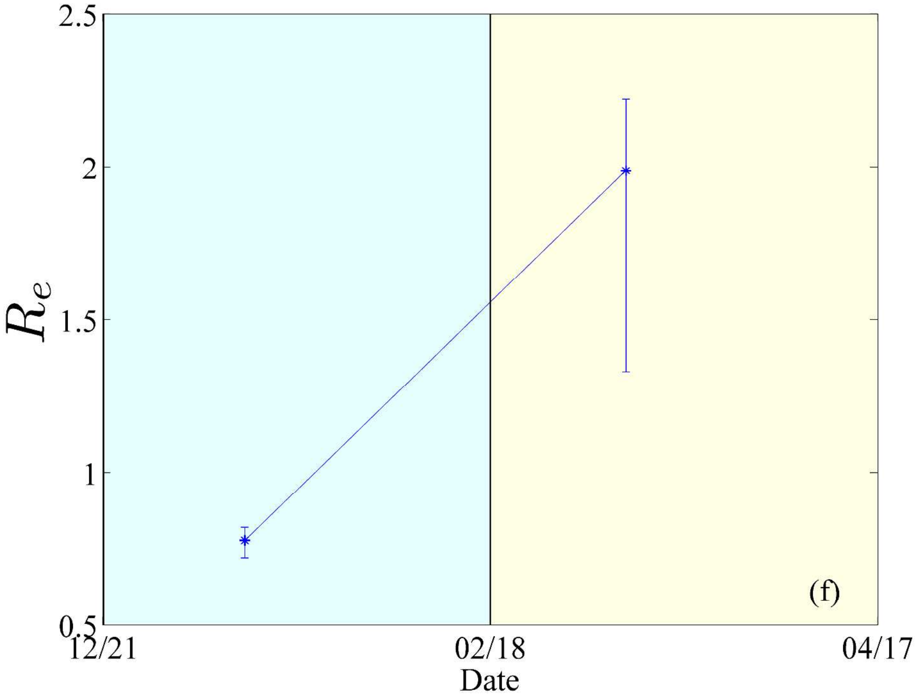


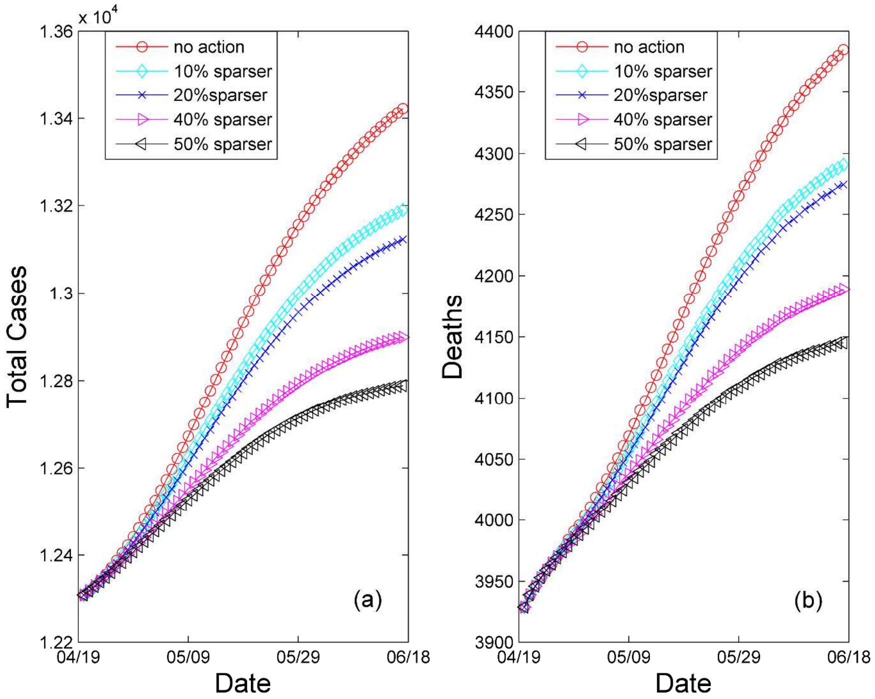
$p_{S\to E}$
0.1
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
12/21
02/18
04/17
Date
(b)


0.18
0.16
0.14
0.12
0.1
0.08
$p_{I\rightarrow R}$
(c)
12/21
02/18
04/17
Date


0.35
0.3
0.25
0.2
$p_{I\to D}$
12/21
02/18
04/17
Date
(d)


0.45
0.4
0.35
0.3
$p_{D/I}$
(e)
12/21
02/18
04/17
Date


2.5
2
1.5
1
0.5
$R_e$
(f)
12/21
02/18
04/17
Date



Forecasting of the evolution of the epidemic from April 18 to June 17, 2015 under different control scenarios. Network density values were compared to the density of the social network estimated for the period February 18-April 17, 2015. (a) Total Cases, (b) Deaths. The "no further action" scenario is also depicted.