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Ebola virus disease outbreak in Nigeria: Transmission dynamics and rapid control

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ABSTRACT

International air travel has already spread Ebola virus disease (EVD) to major cities as part of the unprecedented epidemic that started in Guinea in December 2013. An infected airline passenger arrived in Nigeria on July 20, 2014 and caused an outbreak in Lagos and then Port Harcourt. After a total of 20 reported cases, including 8 deaths, Nigeria was declared EVD free on October 20, 2014. We quantified the impact of early control measures in preventing further spread of EVD in Nigeria and calculated the risk that a single undetected case will cause a new outbreak. We fitted an EVD transmission model to data from the outbreak in Nigeria and estimated the reproduction number of the index case at 9.0 (95% confidence interval [CI]: 5.2–15.6). We also found that the net reproduction number fell below unity 15 days (95% CI: 11–21 days) after the arrival of the index case. Hence, our study illustrates the time window for successful containment of EVD outbreaks caused by infected air travelers.

1. Introduction

Air travel allows Ebola virus disease (EVD) to spread internationally (Gomes et al., 2014; Bogoch et al., 2015). Nigeria experienced an outbreak of EVD with the arrival of an infected air traveler at the international airport in Lagos on July 20, 2014 (Shuaib et al., 2014; Fasina et al., 2014). The traveler had been exposed to EVD in Liberia, had symptoms during his journey, and died on July 25, 2014, after being admitted to a private hospital in Lagos. Although authorities responded to the outbreak rapidly, there were an additional 19 EVD cases in Lagos and a large city in the south of Nigeria, Port Harcourt. The World Health Organization (WHO) declared Nigeria EVD free on October 20, 2014, after no new cases had been detected for 42 days (World Health Organization, 2014).

Analyses of data from the EVD outbreak in Nigeria can provide important information about the impact of the sudden introduction of EVD in large cities and on the control measures needed to stop such outbreaks. The basic reproduction number R_0 is defined as the average number of secondary infections generated by an infectious index case at the beginning of an outbreak (Heffernan et al., 2005). The aim of control interventions is to reduce the net reproduction number R_t during an outbreak (also called the effective or instantaneous reproduction number) below unity so that the outbreak eventually ends. Studying the change in R_t during the course of an outbreak provides useful information on the effectiveness of the control measures that were implemented (Chowell et al., 2004; Althaus, 2014; Camacho et al., 2014).

In this study, we fitted an EVD transmission model to the reported daily numbers of incident cases and deaths during the outbreak in Nigeria. This allowed us to estimate the basic reproduction number R_0, and to describe how the net reproduction number R_t changed after control interventions were implemented. We then compare the risks of an outbreak from a single undetected case in Nigeria and the other West African countries with ongoing EVD transmission.

2. Methods

2.1. Model

We applied an EVD transmission model that we used to estimate the reproduction number of EVD in Guinea, Sierra Leone and Liberia (Althaus, 2014). EVD transmission follows SEIR (susceptible-exposed-infectious-recovered) dynamics (Fig. 1) and

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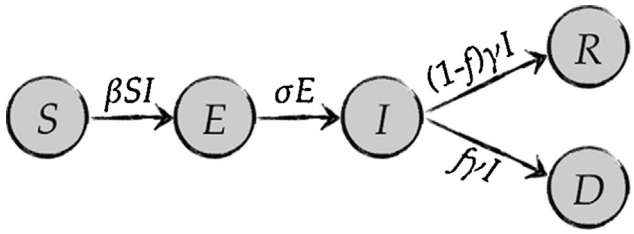

Fig. 1. Schematic illustration of the EVD transmission model. Susceptible individuals S become infected by infectious individuals I at rate β. They then move through an incubation period (E) at rate σ before they become infectious individuals I. Infectious individuals I recover or die at rate γ. The case fatality rate is given by f.

can be described by the following set of ordinary differential equations (ODEs):

$$\frac{dS}{dt} = -\beta(t)SI, \quad (1)$$

$$\frac{dE}{dt} = \beta(t)SI - \sigma E, \quad (2)$$

$$\frac{dI}{dt} = \sigma E - \gamma I, \quad (3)$$

$$\frac{dR}{dt} = (1-f)\gamma I, \quad (4)$$

$$\frac{dD}{dt} = f\gamma I. \quad (5)$$

After infection, susceptible individuals S enter the exposed class E before they become infectious individuals I and either recover (R) or die (D). The average durations of incubation and infectiousness are given by $1/\sigma$ and $1/\gamma$, respectively. f is the case fatality rate. The transmission rate before the introduction of control interventions was assumed to be constant, i.e., $\beta(t) = \beta_0$. Upon the implementation of control measures at time τ, the transmission rate was assumed to decay exponentially: $\beta(t) = \beta_0 e^{-k(t-\tau)}$ (Lekone and Finkenstädt, 2006). The basic and net reproduction numbers are given by $R_0 = \beta_0 S(0)/\gamma$ and $R_t = \beta(t)S(t)/\gamma$, respectively.

We assumed the outbreak started with a single infected case in a large susceptible population ($I(0) = 1$ and $S(0) = 10^6$). As long as the number of cases is small compared to the total population size, the exact number of susceptible individuals does not need to be known to estimate the model parameters. The ODEs were solved numerically in the R software environment for statistical computing (Development Core Team, 2014) using the function *ode* from the package *deSolve*.

We assumed the observed daily numbers of incident cases and deaths to be Poisson distributed (Nishiura and Chowell, 2014; Camacho et al., 2014; Ebola Response Team, 2014) to derive maximum likelihood estimates (MLEs) of the following model parameters (Bolker, 2008): the baseline transmission rate β_0, the rate k at which control measures reduce transmission, and the case fatality rate f. The average durations of incubation ($1/\sigma$) and infectiousness ($1/\gamma$) were fixed to values obtained from other data sets (2.2). We also set $\tau = 3$ days as the implementation of control measures began on July 23, 2014 (Shuaib et al., 2014). We used the optimization algorithm by Nelder & Mead, which is implemented in the function *optim*.

We derived simulation based 95% confidence intervals (CIs) for the model curve making use of the asymptotic normality of MLEs (Mandel, 2013). We also constructed 95% prediction intervals (PIs) for the cumulative number of cases and deaths. The algorithm was as follows:

1 Simulate $n = 10,000$ values, $\theta_1, \ldots, \theta_n \sim N(\hat{\theta}, \Sigma)$, where $\hat{\theta}$ is the MLE of the unknown model parameters with associated variance–covariance matrix Σ, using the function *rmvnorm* from the package *mvtnorm*.
2 For each θ_i, solve the system of ODEs to obtain the model curves for the cumulative number of infected cases and deaths. For each time-point t, use the 2.5% and 97.5% quantiles from these bootstrap samples to construct the point-wise CIs for the model.
3 For each epidemic trajectory, simulate a vector of daily incident cases from the sampling model, assuming they are Poisson distributed. For each time-point t, use the resulting bootstrap sample of the cumulative number of cases to construct the 95% PI. Proceed similarly for the number of deaths.

2.2. Data

Daily incidence of symptom onset and death were derived from the published reports about confirmed ($n = 19$) and probable ($n = 1$) EVD cases (Shuaib et al., 2014; Fasina et al., 2014). We extended the data set from the time of death of the last case to the date that WHO declared Nigeria EVD free (October 20, 2014) with zero counts for the number of incident cases and deaths.

The mean incubation period of EVD was based on the reported cases from the EVD outbreak in Zaire in 1976 (Breman et al., 1978; Breman and Johnson, 2014). We only used the time of symptom onset after person-to-person contact ($n = 109$, range: 2–21 days). Fitting a gamma distribution to the data resulted in a mean incubation period of 9.31 days (shape: 3.04; rate: 0.33).

The mean duration of the infectious period of EVD was calculated from the reported cases in the early transmission chain of the outbreak in Guinea. Baize et al. (2014) described the dates of onset of symptoms and death in 17 patients. We assumed that the infectious period was the difference between these two dates (range: 4–17 days). Fitting a gamma distribution to the data resulted in an average infectious period of 7.41 days (shape: 5.29; rate: 0.71).

3. Results

Fitting the transmission model to the data illustrates the variation around the expected number of cases and deaths for a small EVD outbreak, as observed in Nigeria (Fig. 2). The model provides a good description of the cumulative number of deaths. However, the model shows an earlier and slower increase in the cumulative number of cases, compared to the rapid rise in cases that was observed between 8 and 13 days after the arrival of the index case in Lagos. This discrepancy could be a result of stochastic effects or our assumptions about the transmissibility of EVD (see Section 4). The maximum likelihood estimate (MLE) of the baseline transmission rate β_0 was 1.22×10^{-6} per individual per day (95% CI: 0.70×10^{-6}–2.10×10^{-6} per individual per day). This corresponds to a basic reproduction number $R_0 = 9.01$ (95% CI: 5.22–15.55). The rate at which control measures reduce transmission was estimated at $k = 0.19$ per day (95% CI: 0.10–0.38 per day), and the case fatality rate at $f = 0.39$ (95% CI: 0.14–0.71).

The Nigerian Federal Ministry of Health, the Lagos State government and international partners activated an Ebola Incident Management Center on July 23, 2014 (Shuaib et al., 2014). Based on our estimates of the baseline transmission rate β_0 and the rate k at which control interventions reduce transmission, we calculated the decrease in the net reproduction number R_t following the introduction of control measures that included case isolation, contact tracing and surveillance (Fig. 3). We estimated that R_t dropped below unity 15 days (95% CI: 11–21 days) after the arrival of the index case, that is, 12 days after control measures were implemented. This is about one serial interval after the index case arrived at the airport in Lagos (Ebola Response Team, 2014) and explains the small number of secondary and tertiary cases that was observed in this outbreak (Shuaib et al., 2014; Fasina et al., 2014).