Rapid drop in the reproduction number during the Ebola outbreak in the Democratic Republic of Congo

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ABSTRACT

In 2014, the Democratic Republic of Congo (DRC) experienced an outbreak of Ebola virus disease (EVD) with 69 reported cases. I fitted an EVD transmission model to data of this outbreak and estimated the basic reproduction number $R_0 = 5.2$ (95% confidence interval [CI]: 4.0–6.7). The model suggests that the net reproduction number R_t fell below unity 28 days (95% CI: 25–34 days) after the onset of symptoms in the index case. This illustrates that early outbreak detection and rapid implementation of control interventions are crucial for preventing wider spread of EVD in rural areas.

Keywords: Ebola virus disease, outbreak, basic reproduction number, mathematical model, Democratic Republic of Congo

INTRODUCTION

The Democratic Republic of Congo (DRC) experienced a confined outbreak of Ebola virus disease (EVD) in rural areas of Équateur province. The first case became ill on July 26, 2014 and the last case started to show symptoms on October 4, 2014, resulting in a total of 69 reported cases (Maganga et al., 2014). The index case was a pregnant woman who died later. A doctor and three health care workers performed a postmortem cesarean section, and all of them became infected and died. In total, 21 cases during the first 24 days of the outbreak had direct contact to the index case (Maganga et al., 2014). However, it remains unclear how many of those 21 cases acquired the infection from the index case, and not through other secondary cases.

A better understanding of the transmission dynamics of the 2014 EVD outbreak in DRC can provide crucial information for controlling current and future EVD epidemics in rural areas. The average number of secondary infections generated by an infectious index case at the beginning of an outbreak is described by the basic reproduction number R_0 (Heffernan et al., 2005). An outbreak can be brought under control once the net reproduction number R_t (also called the effective or instantaneous reproduction number) drops below unity. Several analyses of R_0 and R_t for previous EVD outbreaks have given detailed insights into the transmission dynamics and the effectiveness of control interventions (Chowell et al., 2004; Althaus, 2014; Camacho et al., 2014; Althaus et al., 2015).

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In this study, I fitted an EVD transmission model to the reported daily numbers of incidence cases during the outbreak in DRC. This allowed me to quantify the transmission dynamics of this outbreak, provide an estimate of R_0, and calculate the date the outbreak was brought under control.

METHODS

I applied a previously published EVD transmission model to obtain maximum likelihood estimates (MLE) of transmission and control parameters. The full details of the model and fitting method are described in Althaus et al. (2015). In brief, EVD transmission was described assuming SEIR (susceptible-exposed-infectious-recovered) dynamics. I assumed that the transmission rate decays exponentially after the implementation of control measures.

The daily incidence of onset of symptoms was dervied from the study by Maganga et al. (2014). I extended the data set from the time of symptom onset in the last case to the date that the World Health Organization (WHO) declared the outbreak in DRC to be over (November 20, 2014) with zero counts for the number of incident cases. The average durations of incubation (9.31 days) and infectiousness (7.41 days) were fixed to values from previous outbreaks (Althaus et al., 2015).

Assuming the observed daily numbers of incident cases to be Poisson distributed (Camacho et al., 2014), I derived MLEs of the following three parameters: the baseline transmission rate β_0, the time τ at which control interventions were implemented, and the rate k at which control interventions reduced transmission. Those parameters were used to calculate the basic reproduction number R_0, the net reproduction number R_t and the time at which R_t dropped below unity. I derived simulation based 95% confidence intervals (CIs) for the model curve making use of the asymptotic normality of MLEs (Mandel, 2013), and constructed 95% prediction intervals (PIs) for the daily incidence and cumulative number of cases. All analyses were performed in the R software environment for statistical computing (R Development Core Team, 2014).

RESULTS AND DISCUSSION

Fitting the transmission model to the data provided a good description of the EVD outbreak in DRC (Figure 1). The daily incidence of new cases developing symptoms peaked a bit less than four weeks after the start of the outbreak. The MLE of the basic reproduction number was $R_0 = 5.15$ (95% CI: 3.95–6.69), which is higher than estimates from other, larger outbreaks (Chowell et al., 2004; Althaus, 2014; Camacho et al., 2014). However, the number is lower than the value suggested in the study by Maganga et al. (2014) which found that 21 patients had direct contact with the index case. It is important to note that the time from onset of symptoms to death in the index patient (16 days) is substantially longer than the average duration of infectiousness in the model (7.4 days). Hence, the number of secondary cases generated by the index case could be more than twice as high as the estimated R_0, indicating a potential superspreading event during this outbreak (Althaus, 2015).

The time at which control interventions started to reduce transmission was estimated at 14.3 days (95% CI: 5.2–23.4 days) after the start of the outbreak (Figure 2). This time point is before the death of the index cases (16 days after onset of symptoms) and

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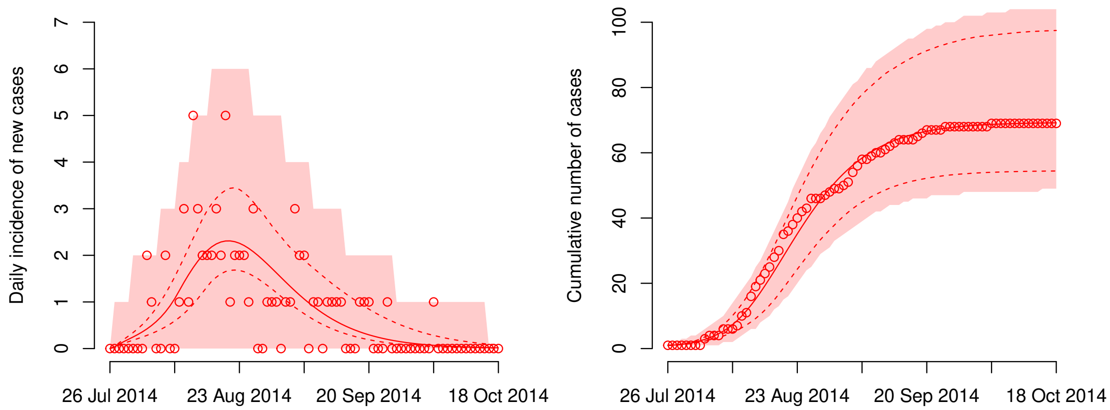

Figure 1. Dynamics of Ebola virus disease (EVD) outbreak in the Democratic Republic of Congo (DRC). Model fits of daily incidence (left panel) and cumulative numbers (right panel) of cases are shown together with reported data (circles). The best-fit model (solid lines) is given together with the 95% confidence intervals (dashed lines). The shaded areas correspond to the 95% prediction intervals.

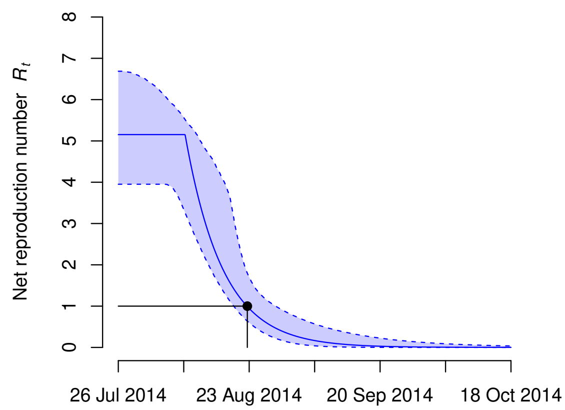

Figure 2. Net reproduction number R_t during the Ebola virus disease (EVD) outbreak in the Democratic Republic of Congo (DRC). The maximum likelihood estimates of the net reproduction number R_t (solid line) are shown together with the 95% confidence intervals (dashed lines). The black dot denotes the time at which R_t dropped below unity (27.6 days after the start of the outbreak).

the subsequent cesarean section that lead to four secondary cases. However, the CIs around the estimated time point are wide and are also consistent with an introduction of control interventions that start one week after the death of the index case. Following the introduction of control measures, the net reproduction number R_t dropped below unity 27.6 days (95% CI: 24.7–33.7 days) after the start of the outbreak. This time point roughly coincides with the date at which the modeled daily incidence of new cases is highest (Figure 1, left panel).

This is the first study inferring the transmission dynamics of the 2014 EVD outbreak in DRC using mathematical modeling. The model is based on an established framework that was applied for the analysis of a limited urban outbreak of EVD in Nigeria (Althaus et al., 2015). Nevertheless, there are a number of limitations. First, the model does not

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distinguish between transmission in the community and in health-care settings. Second, the model cannot capture the separate contribution of different control interventions, such as case isolation, protection of health care workers, and contact tracing, in reducing transmission. Third, the analysis is restricted to incidence data of symptom onset. Adding an additional variable for incidence of death could result in more accurate parameter estimates.

In summary, this study provides a detailed quantitative description of the transmission dynamics of the 2014 EVD outbreak in DRC. The study illustrates how mathematical modeling can complement epidemiological descriptions of EVD outbreaks. The results suggest that the net reproduction number R_t started to fall two weeks after onset of symptoms in the index case, and that it dropped below unity another two weeks later. This highlights the importance of a rapid response to EVD outbreaks in rural areas in order to prevent further spread.

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