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# A one-year effective reproduction number of the 2014–2015 Ebola outbreaks in the widespread West African countries and quantitative evaluation of air travel restriction measure

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**KEYWORDS**
Effectiveness;
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Transboundary

**Summary** *Background:* The 2014–2015 Ebola outbreak in West Africa is the largest and longest Ebola Virus Disease (EVD) outbreak in the history, and the virus has escaped across countries and continents via air travel in this outbreak.
*Method:* The interpolated data from WHO Ebola situation reports were used to estimate number of weekly infectious individuals and daily effective reproduction numbers ($R_t$) in Guinea, Liberia and Sierra Leone. A stochastic dynamic model was performed to estimate the risk of EVD importation into the top 20 final destination countries of air travelers departing from within the three epidemic countries, and the effectiveness of air travel restriction was subsequently evaluated.
*Results:* The daily $R_t$ was estimated at 0.72–1.32 in Guinea, 0.62–1.38 in Liberia and 0.81–1.38 in Sierra Leone. The peak of EVD importation probability was observed in early

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November 2014 and the restriction of air travel may mitigate the risk up to 67.7% (95% CI 66.6—68.7).
*Conclusions:* Our results suggest that restriction of air travels is effective in reducing the risk of EVD importation but controlling of the virus at the original affected countries is vitally more important for preventing inter-terrestrial dissemination of EVD.


## 1. Introduction

Ebola disease virus (EDV) was firstly discovered in two inaugural epidemics, in Sudan and Democratic Republic of Congo (DRC), in 1976. Subsequently, 27 occurrences of Ebola virus disease (EVD) outbreaks were observed in the continent of Africa before the occurrence of 2014—2015 outbreaks in West African countries [1]. It was estimated that 22 million residents dwelling in Central and West Africa are at risk of EVD infection [2].

The 2014 epidemics of Ebola virus (originally Zaire ebolavirus) were presumed to initiate in the south of Guinea in December 2013 [3]. However, the World Health Organization (WHO) officially notified the outbreak in Guinea, around three months later, on March 23, 2014 [4]. As the longest, largest, deadliest and most widespread EVD outbreak in the history, the WHO Director-General Margaret Chan declared the epidemic to be a Public Health Emergency of International Concern (PHEIC) for unifying global community in combating the epidemic to be under control [5].

As of March 22, 2015, a total of 24,907 cases have been reported from nine countries to WHO with 10,326 fatal cases (41.5% case-fatality rate) [6]. Majority of the cases were reported from three EVD widespread countries in West Africa namely Guinea, Liberia and Sierra Leone [7]. Others were notified from three African countries (Mali, Nigeria and Senegal) and three other countries outside Africa (Spain, United Kingdom and the United States of America) [6]. However, the importation of an EVD case was still notified in Italy after one year of the epidemics [8]. Interestingly, the imported cases in Italy, Nigeria, Spain, United Kingdom and the United States of America arrived in their countries by mean of air travels [8—14]. Only the cases in Mali and Senegal entered the counties by ground system [15,16]. Moreover, six sevenths of the EVD importing countries, excluding Spain, are in the list of top 20 final destinations of passengers initiating air travel from within the three EVD widespread countries [17]. In this unprecedented outbreak, the notorious virus affected also the cities with major commercial airport [18]. Hence, it is likely that commercial air travel may allow further dissemination of the virus internationally. Particularly, in the case that the epidemics in West African countries are still rising and the airport-based traveler screening are not sufficiently effective.

The present study, thus, aimed to assess daily effective reproduction number of EVD epidemics in Guinea, Liberia and Sierra Leone and quantify the risk of EVD importation into the top 20 final destination countries through commercial air travel departing from the three epidemic countries in West Africa, and finally we tried to evaluate a related control measure namely air travel restriction.

## 2. Materials and methods

### 2.1. Data

Cumulative number of EVD cases during March 25, 2014 to March 22, 2015 were routinely recorded from WHO Ebola Situation Reports web site [19]. Since the number of EVD cases was usually not regularly reported, we interpolated these reported numbers to obtain daily data. The interpolation was carried out with Piecewise Cubic Hermite Interpolating Polynomial (PCHIP) in Matlab software (MathWorks, MA, USA).

### 2.2. Estimating number of infectious individuals and effective reproduction number using SIR model

We estimated time series of EVD infectious cases in Guinea, Liberia and Sierra Leone by implementing the standard Susceptible—Infectious—Recovered (SIR) model where each country was modeled individually. Each country is thus governed by the same SIR dynamics: $S \xrightarrow{\beta I/N} I \xrightarrow{\gamma} R$. Susceptible individuals ($S$) are infected at a rate of $\beta I/N$ where $\beta$ is the Ebola transmission rate, which incorporates the encounter rate between susceptible and infectious individuals together with the probability of transmission, and $N = S + I + R$ is the total number of population in each country. The infectious individuals develop protective immunity (or die) and are thus moved to the removed group ($R$) with the mean duration of the infectious stage $1/\gamma$. The model is based on the following set of deterministic coupled ordinary differential equations:

$$\begin{aligned} \frac{dS}{dt} &= -\frac{\beta}{N} IS \\ \frac{dI}{dt} &= \frac{\beta}{N} IS - \gamma I \\ \frac{dR}{dt} &= \gamma I \end{aligned} \tag{1}$$

The model parameter values are based on reported epidemiological data from recent literature. The mean infectious period ($1/\gamma$) is 7.9 days, and the mean serial interval is 15.3 days [18]. According to the World Bank, total numbers of population ($N$) in Guinea, Liberia and Sierra Leone in 2014 were 1,1745,189, 4,294,077 and 6,092,075, respectively [20]. We assumed that populations in the three countries were fixed throughout the study period. We assumed that the number of removed individuals, $R$, is approximately equal to the number of cumulative reported cases, hence the number of infectious individuals can be

calculated from $I = (1/\gamma)(dR/dt)$. The effective reproduction number ($R_t$) was then estimated from the following formula (see Supplementary Material for detailed derivation)

$$R_t = 1 + \frac{r}{\gamma}, \quad (2)$$

where $r$ is the intrinsic growth rate of the infectious population [21].

## 2.3. Risk estimation of EVD importation and assessment of air travel restriction measure

### 2.3.1. Average weekly number of travelers

We adopted the list of the top 20 final destination countries of air travelers departing from Guinea, Liberia and Sierra Leone from Bogoch et al. [17]. The names of countries and average weekly numbers of travelers are shown in Table 1.

To deal with uncertainty, we stochastically simulated weekly number of travelers with Poisson distribution as $T_{n,t} \approx Pois(\lambda_{n,t})$, where $T_{n,t}$ and $\lambda_n$ refer to simulated number of travelers outbound from the three EVD widespread countries and arriving in country $n$ in week $t$ and average weekly number of passengers arriving in country $n$ in week $t$.

To use as baseline data for risk estimation of EVD importation, we generated weekly numbers of passengers for the whole study period. The stochastic processes were employed under the assumption that traveling behaviors did not alter over time.

**Table 1** Average weekly number of travelers initiating air travel from within Guinea, Liberia and Sierra Leone to top 20 final destination countries (adopted from Bogoch et al. [17]).

| Country | Average weekly traveler |
|---|---|
| Ghana | 1462.02 |
| Senegal | 1204.35 |
| UK | 722.75 |
| France | 595.42 |
| Gambia | 569.80 |
| Côte d'Ivoire | 478.17 |
| Morocco | 438.20 |
| Belgium | 320.53 |
| Nigeria | 241.92 |
| China | 236.60 |
| Mali | 212.87 |
| USA | 169.33 |
| India | 142.66 |
| Kenya | 138.39 |
| Germany | 105.56 |
| Lebanon | 98.70 |
| South Africa | 90.16 |
| Guinea–Bissau | 77.49 |
| Canada | 75.18 |
| Italy | 74.83 |

### 2.3.2. Risk estimation of EVD importation

We assumed that population in each EVD widespread country was homogenously mixed and all individuals had equal chance to travel by commercial air flights. The weekly number of EVD imported cases was stochastically simulated with binomial distribution as $I_{n,e,t} \approx BN\left(T_{n,e,t}, \frac{C_{e,t}}{P_e}\right)$, where $I_{n,e,t}$ and $T_{n,e,t}$ are number of EVD cases and total number of travelers who travel to country $n$ from EVD epidemic country $e$ in week $t$ whereas $P_e$ and $C_{e,t}$ refer to number of populations of EVD epidemic country $e$ [20] and number of total EVD cases in EVD epidemic country $e$ in week $t$, respectively. Subsequently, country-based probability to have at least one internationally imported case in each week was calculated. The model was simulated under worst-case scenario which not any interventions were undertaken.

The EVD importation risk model was stochastically performed in 100,000 simulations in statistical programing language R version 3.2.2 (R development Core Team, Vienna, Austria).

### 2.3.3. Modeling the restriction of air travel outbound from the three EVD widespread countries

A reduction of international air travel outbound from the three EVD widespread countries were previously estimated in a published study at 66, 51 and 85 percent for Guinea, Liberia and Sierra Leone, respectively [17]. We followed these estimates and recalculated the country-based probability to have at least one internationally imported case to illustrate the impact of this intervention.

# 3. Results

## 3.1. EVD cases and interpolation

During a one-year period, cumulative number of EVD cases were consecutively reported. Number of cumulative cases was exponentially increased at early time. At the end of this study, cumulative numbers of cases in Guinea, Liberia and Sierra Leone were 2,429, 9602 and 11,841, respectively. However, the irregularity in the reporting process was observed especially in Liberia. The reported data were thus interpolated. Daily interpolated number of EVD cases in each epidemic country is shown in Fig. 1. In case of Liberia, we created another smoothly interpolated version to encounter the unusual inconsistency of the report (the light blue line in Fig. 1.).

## 3.2. Number of infectious individuals

As illustrated in Fig. 2, the most prominent peak of weekly infectious individuals was observed in Liberia at 15,339 individuals in the week 31 (October 21–27, 2014). However, this steep peak was smoothly interpolated into two different consecutive peaks with 6235 and 5915 infectious individuals in week 25 (September 9–15, 2014) and week 32 (October 28–November 3, 2014), respectively. In the case of Sierra Leone, number of infectious individuals was gradually increased and hit the peak in week 33 (November

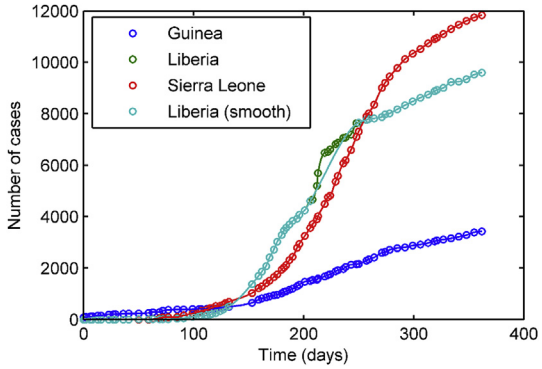


**Fig. 1** Cumulative number of EVD cases during March 25, 2014 to March 22, 2015 as reported to WHO from Guinea (blue circle), Liberia (green circle: actual report, light blue: the smoothly modified version) and Sierra Leone (red circle). The lines show daily interpolation data of the observed data in each country. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

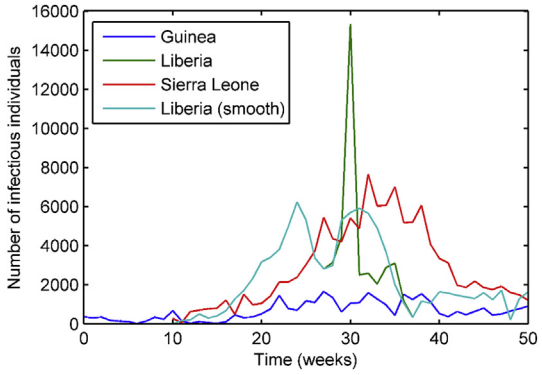


**Fig. 2** The estimated number of weekly EVD infectious individuals in Guinea (blue line), Liberia (green line: simulated from actual WHO report, light blue line: estimated from the smooth interpolated version) and Sierra Leone (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

4—10, 2014) at 7650 individuals before continuously declined with a few sub-peaks in week 36 (November 25—December 1, 2014) and 39 (December 16—22, 2014). Nonetheless, the noticeable peaks were not found in case of Guinea. At the end of the study period, numbers of infectious individuals in Guinea, Liberia and Sierra Leone were estimated at 909, 1643 and 1208 individuals, respectively.

### 3.3. EVD effective reproduction number

Daily effective reproduction numbers calculated using interpolated data in Guinea, Liberia and Sierra Leone throughout the study period are shown in Fig. 3. Fluctuation of the values was illustrated in all study countries and all study period. The range of daily effective reproduction number was between 0.72 and 1.32 in Guinea, 0.62—1.38 in Liberia and 0.81—1.38 in Sierra Leone. On average, the means daily effective reproduction number in the three countries were 1.02 (95% CI 1.01—1.03), 1.04 (95% CI 1.02—1.06) and 1.03 (95% CI 1.02—1.04), respectively. At the end of study period, the daily effective reproduction number was 1.05 in Guinea, 1.18 in Liberia and 0.95 in Sierra Leone.

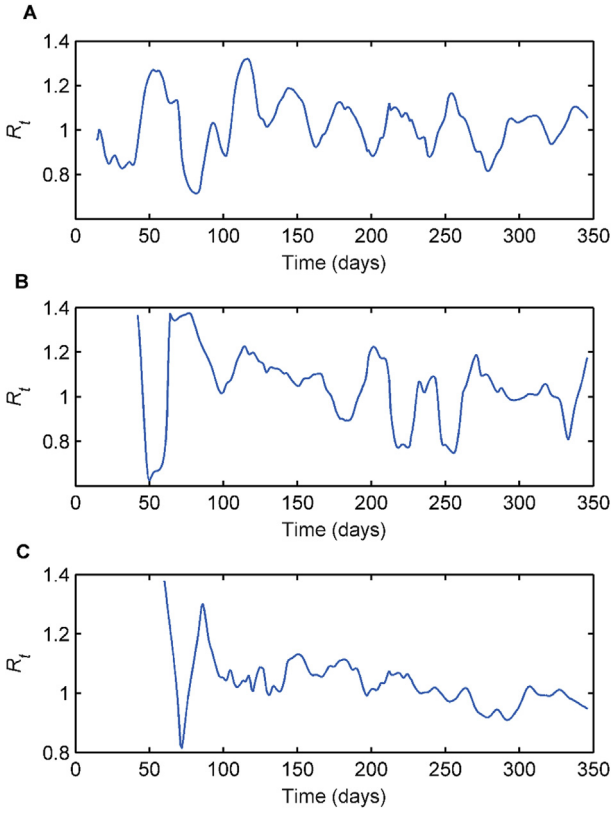


**Fig. 3** Daily effective reproduction number of EVD epidemics in Guinea (A), Liberia (B) and Sierra Leone (C) in the 2014—2015 EVD outbreaks in West Africa.

### 3.4. Risk estimation of EVD importation into the top 20 final destination countries via commercial air travel

Fig. 4 shows the weekly risk to have at least one infected passenger importing into the top 20 final destination countries via commercial air travel under worst-case scenario with no interventions implemented. The risk kept increasing as number of EVD cases in the departing countries increased. The peak of EVD importation probability was observed in week 33 (November 4—10, 2014) at 0.73, 0.67 and 0.49 for the top three countries of destination namely Ghana, Senegal and United Kingdom. At the end of this study, the importation probability in these three countries declined to 0.28, 0.23 and 0.14, respectively. In other 17 countries, the probability of EVD importation ranged between 0.00 and 0.36. To provide a better spatial visualization, the map of EVD importation probability was shown in Fig. 5.

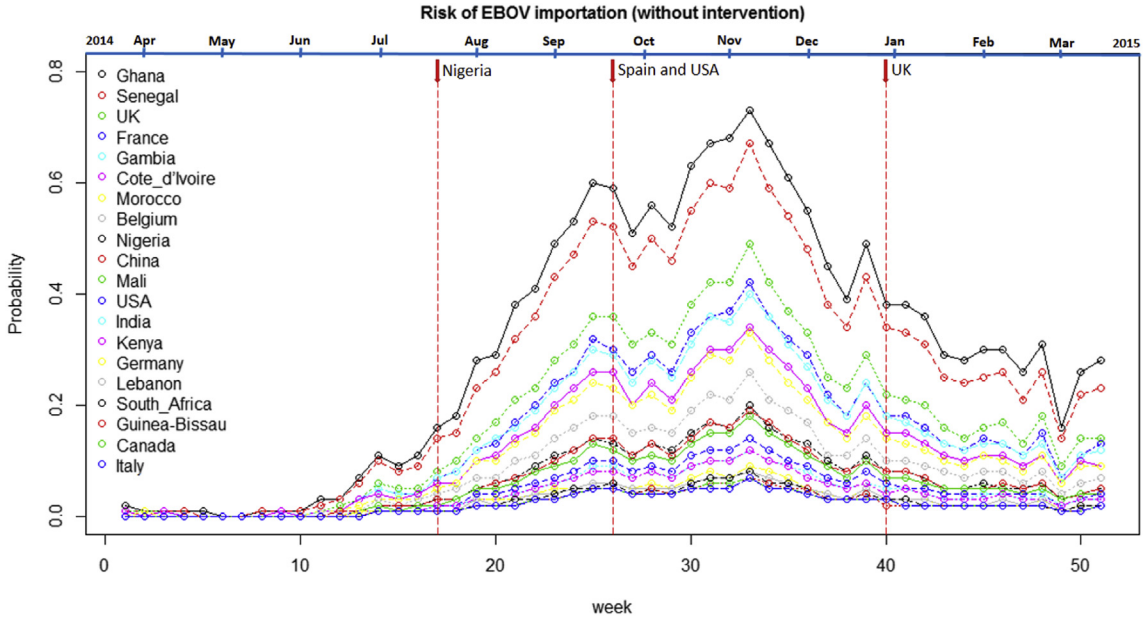


**Fig. 4** Stochastic simulation results of EVD importation risk. The model was simulated, under worst-case scenario with no interventions, for commercial air travelers departing from Guinea, Liberia and Sierra Leone to the top 20 final destination countries. The vertical arrows and dashed lines indicate the EVD importation weeks in the identified countries [8—12].

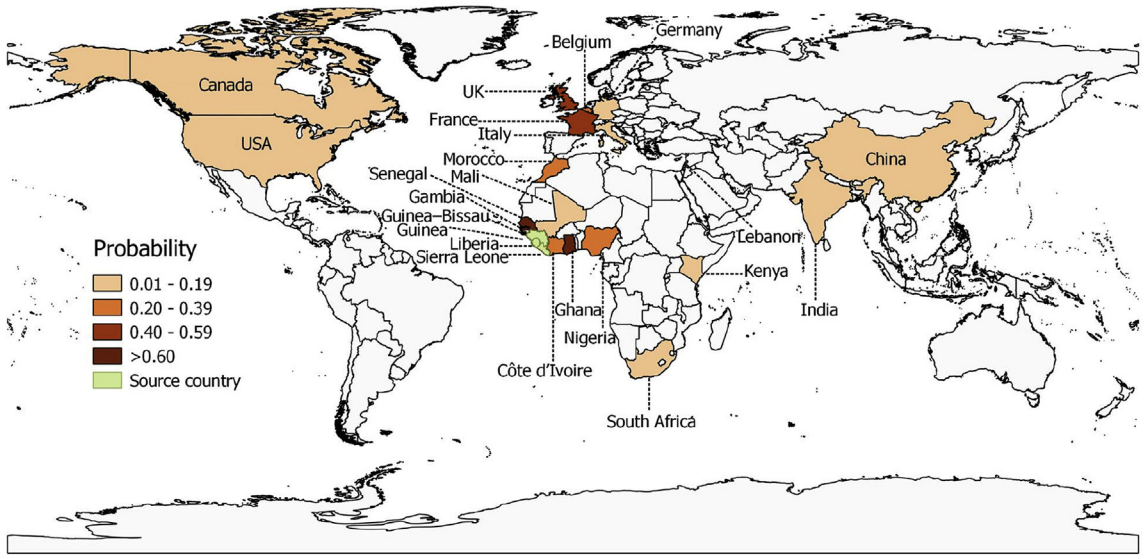


**Fig. 5** The world map illustrating the EVD importation probability into the top 20 final destination countries in the peak week (week 33, November 4—10, 2014).

### 3.5. Effectiveness of air travel restriction measure

In our intervention simulations, air travel volume was assumed to be restricted throughout the study period. In the top three countries of destination (Ghana, Senegal and the United Kingdom), the highest probability of EVD importation through commercial air travel dropped to 0.35, 0.29 and 0.19 which are accounted as 52.1, 56.7 and 61.2 percent of reduction, respectively. On overall, the risk of EVD importation into all 20 countries in the whole study period was diminished by 67.7% (95% CI 66.6—68.7) after this strategy was implemented. The results of this intervention simulation are demonstrated in Fig. 6.

## 4. Discussion

The present study estimates the effective reproduction number of the unprecedented 2014—2015 Ebola outbreaks in the widespread affected countries namely Guinea, Liberia and Sierra Leone in a one-year period. A risk estimation of the Ebola virus importation was carried out for the top 20 countries traveled by the populations of these three epidemic countries using commercial flights.

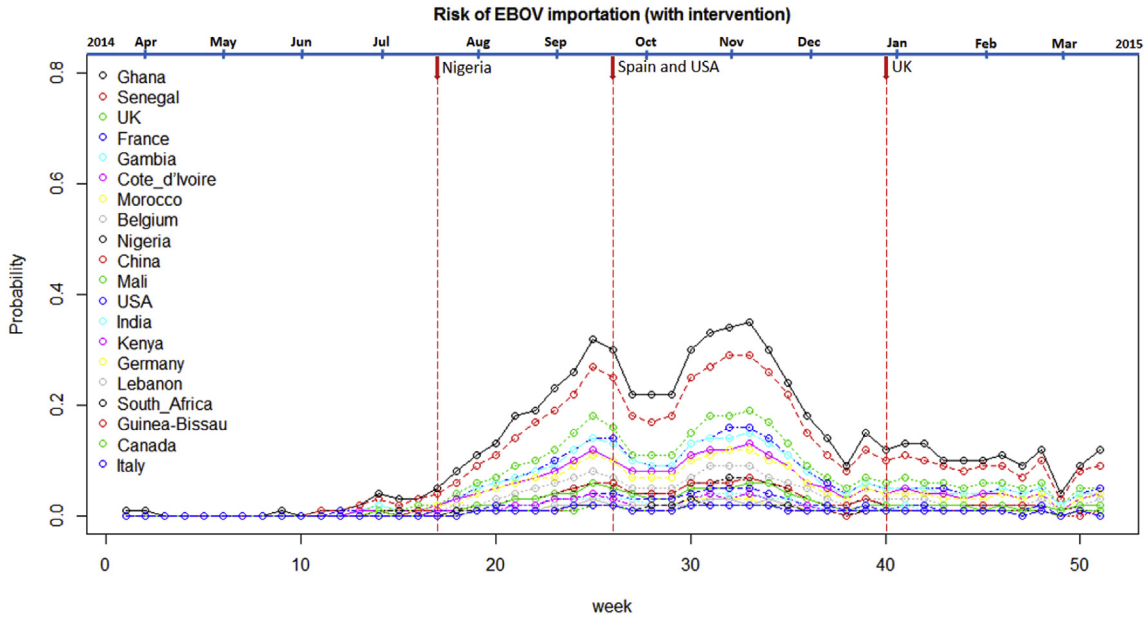


**Fig. 6** Intervention simulation of air travel volume restriction strategy implemented to reduce the risk of EVD importation into the top 20 final destination countries. The number of passengers decreased by 66, 51 and 85 percent for air travelers departing from Guinea, Liberia and Sierra Leone, respectively. The vertical arrows and dashed lines indicate the EVD importation weeks in the identified countries [8—12].

Subsequently, the effectiveness of air travel restriction measure was quantitatively assessed.

In the present study, we found that daily effective reproduction numbers of EVD infection in Guinea, Liberia and Sierra Leone kept fluctuating during the study period especially in the first 220 days (until the end of October, 2014). The marginal fluctuation of reproduction number in the same period was also described in a previous study [22]. Focusing on this period, the reproduction numbers calculated in our study for Guinea (0.72—1.32) and Sierra Leone (0.81—1.38) were broadly comparable with the recent study (Guinea: 1.08—1.31 and Sierra Leone: 1.28—1.70) [22] even though our values were a bit lower. However, our effective reproduction number in Liberia is much less than that proposed in the previous study [22] (0.62—1.38 Versus 2.09—2.22). Please note, however, that the authors in ref. [22] estimated the effective reproduction number by using the formula $R_t = exp(rT)$, where $r$ is the per capita growth rate of the cumulative case number in the Richards model and $T$ is the generation interval of the disease. This expression generally provides an upper bound for effective reproduction number [23].

Previously, some studies tried to assess the risk of EVD importation into different countries, for instances, Australia [24], China [25], Malaysia [26] and Latin American countries [27]. Some others focused on how EVD propagates through the aviation travel [17,18]. However, to our knowledge, this study is the first to use the interpolated cumulative EVD cases in the original EVD widespread epidemic countries to estimate number of infectious individuals and perform a real-time estimation of EVD importation risk throughout a year after the outbreak was officially notified [13].

As illustrated in Fig. 4, the EVD began to spill over into other African country namely Nigeria in late July 2014 [12] which is the period that probability of importation started to climb up. In Nigeria, the outbreak initiated with only one infectious airline passenger arriving in the country and then spread out [28,29]. It was estimated that the reproduction number of this index case is around 9.0 [29]. Eventually, EVD killed 8 persons out of 20 reported cases in Nigeria [29]. In late September 2014 which is the point that the probability of EVD importation in our model just reached the first peak, the virus jumped across the continents to Spain [8] and the United States of America [10]. In Spain, it was marked as the first acquired EVD infection outside Africa [8]. These events threatened global community of a potential EVD pandemic with high mortality rate [22,30]. Nonetheless, the ultimate peak of importation risk was in November 2014 but there were no EVD cases escaping West Africa reported during this period. However, we found the exportation of an EVD case again to United Kingdom at the end of the year 2014 [11], one week after a small peak estimated in our model. As stated in the methodology, our model was carried out under the condition that no interventions were undertaken to halt the spread of EVD beyond the territories of epidemic countries. In fact, many control measures were seriously implemented such as screening of travelers for fever in the airports [31], reducing or canceling flights from and to the epidemic counties [17] or even banning visas from affected countries [24]. These interventions may alleviate the risk whereas our model proposes the worst-case scenario which may, at least, help to identify the critical period that one must urgently prepare and allocate the necessary resources for. Besides, for the sake of simplification, the present simulation did not take into account other possible routes of EVD

exportation from the epidemic countries such as roads, navy ships or connecting flights [27]. Thus, the actual risk might be higher than what we estimated.

In the final step, we evaluated the effectiveness of air travel restriction in the control of EVD spread into the top 20 countries of destination. On overall, we suggest that this measure may reduce the risk of EVD importation by two thirds. However, we did not take into account other control measures at the airports like entry or exit screening of passengers. A previous study argues that self-reporting of symptoms and thermos-scanning at the airports have failed to stop the international spread of SARS and pandemic influenza H1N1 in the past epidemics [14]. The reliability of such systems is still questionable. Moreover, we simply assumed that anyone in the country can fly but this is apparently not realistic due to difference in socioeconomic status among people in each country. Furthermore, volume of flight passengers during the year is highly dynamic due to many factors. Our model may fail to capture all of these complexities but we found that the risk of importation was reduced substantially with air travel restriction. In contrast, it was argued with the experience from other large outbreaks of infectious diseases like SARS and pandemic influenza or even AIDS (in 1980s) that the ban or restriction of air travel did not work and even worsened the situations [32]. In addition, scientific evidences supporting this control measure are always insufficient [32]. However, the restriction of air travel may help to delay the spread and buy the time for international community to prepare for the possible global pandemic.

We faced at least three potential limitations in the present study. First, the quality of outbreak data in the three EVD widespread countries was poorly collected and managed by local authorities. Numbers of cases were reported while case definitions were often reclassified while retrospective investigation as well as data cleaning were ongoing [33]. According to WHO Ebola Response Roadmap Situation Report update, number of EVD reported cases in Liberia was suddenly increased from 4665 on October 23, 2014 [23] to 6535 in the next report on October 27, 2014 [24] which is only four days after. These two thousand uprising cases may result from the accumulation of the cases during the missing days and were counted at once. We thus use the smooth interpolation to make our model more realistic. Moreover, the scarcity of confirmed laboratory results may involve high proportion of suspected and probable cases in the official report [33]. On the other hand, underreported cases and deaths were also likely due to lacking of effective case finding system and public collaboration in these affected poor countries. This may affect and bias the case number estimation, resulting in the bias of our importation risk assessment. Second, our model partly depends on some static data which are highly dynamic including numbers of population in the affected countries and numbers of air travelers as these data were not available in a timely fashion. We thus employed a stochastic model to deal with this uncertainty.

Third, the mathematical model itself is massively relied upon the assumptions and simplifications [34]. Indeed, reality is far more complex than what we simulated in the model. The microbes always evolve and interact with environment and other organisms. Anthropological activities as well as environmental changes are also largely dynamic. This complexity is too difficult to model and predict. Most epidemiological models are thus still based on only one interested pathogen causing an outbreak in a well-defined population which is somehow not realistic and may lead to exaggerated public health responses [35], for example, in the case of the 2003 SARS epidemic [36] and the 2009 influenza pandemic [37]. The epidemic models should be interpreted and applied together with the field empirical data.

In conclusion, our proposed modeling methods can be promptly applied in the possible upcoming outbreaks of Ebola or other emerging and reemerging diseases of potential global concern, such as Zika virus disease, Yellow fever, Lassa fever, etc. A reliable dataset may increase the accuracy of the model. Our results suggest that restriction of air travels may reduce the risk of EVD importation but controlling of the virus at the original affected countries is more important for preventing inter-terrestrial dissemination of EVD.

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## Conflict of interest

The authors declare that there are no conflicts of interest.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tmaid.2016.06.011.

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