

• W is a spatiatemporal spread of the 2014 outbreak of Ebola virus disease in Liberia and the effectiveness of non-pharmaceutical interventions: a computational modelling analysis

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Summary

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Correspondence to: Prof Alessandro Vespignani, Laboratory for the Modeling of Biological and Socio-Technical Systems, Northeastern University, Nightingale Hall, Suite 132, 360 Huntington Avenue, Boston, MA 02115, USA a.vespignani@neu.edu Background The 2014 epidemic of Ebola virus disease in parts of west Africa defines an unprecedented health threat. We developed a model of Ebola virus transmission that integrates detailed geographical and demographic data from Liberia to overcome the limitations of non-spatial approaches in projecting the disease dynamics and assessing nonpharmaceutical control interventions.

Methods We modelled the movements of individuals, including patients not infected with Ebola virus, seeking assistance in health-care facilities, the movements of individuals taking care of patients infected with Ebola virus not admitted to hospital, and the attendance of funerals. Individuals were grouped into randomly assigned households (size based on Demographic Health Survey data) that were geographically placed to match population density estimates on a grid of 3157 cells covering the country. The spatial agent-based model was calibrated with a Markov chain Monte Carlo approach. The model was used to estimate Ebola virus transmission parameters and investigate the effectiveness of interventions such as availability of Ebola treatment units, safe burials procedures, and household protection kits.

Findings Up to Aug 16, 2014, we estimated that 38.3% of infections (95% CI 17.4–76.4) were acquired in hospitals, 30.7% (14.1–46.4) in households, and 8.6% (3.2–11.8) while participating in funerals. We noted that the movement and mixing, in hospitals at the early stage of the epidemic, of patients infected with Ebola virus and those not infected was a sufficient driver of the reported pattern of spatial spread. The subsequent decrease of incidence at country and county level is attributable to the increasing availability of Ebola treatment units (which in turn contributed to drastically decreased hospital transmission), safe burials, and distribution of household protection kits.

Interpretation The model allows assessment of intervention options and the understanding of their role in the decrease in incidence reported since Sept 7, 2014. High-quality data (eg, to estimate household secondary attack rate, contact patterns within hospitals, and effects of ongoing interventions) are needed to reduce uncertainty in model estimates.

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Introduction

The exponential increase of Ebola virus disease cases in Sierra Leone, Liberia, and Guinea during the months of August and September, 2014, defines an unprecedented health threat to west Africa. A massive international response necessitating the large-scale deployment of human and capital resources is needed to stop the epidemic. Such efforts would benefit from quantitative predictions about the growth of the epidemic and the effectiveness of potential containment or mitigation strategies. According to WHO and the Liberian Ministry of Health and Social Welfare reports,12 7069 cases and 2964 deaths were recorded in Liberia by Nov 17, 2014. with 341 cases and 170 deaths in health-care workers. Since September, 2014, the recorded number of cases has not followed the initial exponential growth trend reported in the early phase of the outbreak, and the epidemic might be waning in parts of Liberia.2 In recent years, mathematical modelling at very detailed spatial

resolutions, sometimes down to the level of single individuals, has been tailored to make projections for policy makers using population-specific sociodemographic features of the population.³⁻⁸

Recently published data on Ebola virus transmission9-13 have been key in motivating and informing the strong international response to the epidemic. We propose an approach that can overcome some of the limitations of those early approaches, namely the homogeneous mixing assumption in all settings relevant to Ebola virus disease transmission and lack of spatial structure, which might result in overestimation of disease incidence. We developed a spatial agent-based model that integrates sociodemographic data for Liberia to estimate the relative importance of the main settings for Ebola virus disease transmission, which are within households, in the general community (mainly corresponding to close relatives, in the case of Ebola virus disease), in hospitals, and at funerals during burial ceremonies. We simulated

the Ebola virus disease epidemic in a synthetic population in which every household in Liberia is explicitly represented. The model includes hospitals and clinics treating patients with Ebola virus disease up to mid-August, 2014, and Ebola treatment units in the subsequent period, and the risk of spread to health-care workers working at them. We used the model to project the spatiotemporal spreading of the disease and to disentangle the effect of Ebola treatment unit availability, safe burial procedures, and the distribution of household protection kits in the aversion of Ebola virus disease cases.

Methods

Model structure

The Ebola virus disease natural history model is adopted from Legrand and colleagues:14 susceptible individuals can acquire infection after contact with an infectious individual and become exposed without symptoms; at the end of the latent period infectious and symptomatic individuals can transmit infection at home to both household members and close relatives. Infectious individuals at home then might either be admitted to hospital, die, or recover. Individuals admitted to hospital might also either die or recover. Deceased individuals might transmit infection during their funeral (to household members and relatives belonging to additional households) and are then removed from the model. To account for the spatial spread of the epidemic, we explicitly modelled the movements of individuals, including patients not infected with Ebola virus, seeking assistance in health-care facilities, the movements of individuals taking care of patients infected with Ebola virus not admitted to hospital, and the attendance of funerals. Individuals were grouped into randomly assigned households whose size was based on Demographic Health Survey data and were geographically placed to match population density estimates on a grid of 3157 cells covering the country. A full description of the synthetic population and the transmission model is in the appendix.

Disease transmission

Most Ebola virus disease transmission parameters used in the model were from a study of the present outbreak by the WHO-led team¹⁵ and are summarised in table 1. The model accounts for three routes of transmission: transmission in households and in the general community (corresponding to additional households) when the infected individuals are at home, transmission in hospitals, and transmission during funerals (to household and additional household members). In general hospitals both health-care workers and patients not infected with Ebola virus are exposed to the risk of contracting the disease. Beginning in Aug 15, 2014, the model accounted for the increasing number of hospital beds specific for patients infected with Ebola virus in Ebola treatment units. The number of available beds in Ebola treatment units increases over time according to data reported by the WHO (appendix). Importantly, after August, 2014, patients with symptomatic Ebola virus disease were no longer admitted to general hospitals but only to Ebola treatment units where they could transmit the infection only to health-care workers (with probability 0.05% with respect to general hospitals). Moreover, we assumed that safe burials increase linearly over time from 0% on Aug 15, 2014, to 90% on Oct 15, 2014. In the model, three key parameters have to be estimated for the present outbreak, namely β_{i} (transmission rate in hospitals), β_{i} (transmission rate between household members, including their contacts with the deceased during burial ceremonies), and σ (scaling factor for the transmission rate in the general community relative to β_f).

Model calibration

Simulations were calibrated to begin with 24 initial Ebola virus disease-related deaths by June 16, 2014, matching an early report from WHO. To estimate the three key model parameters, we used a Markov chain Monte Carlo approach exploring the likelihood of the recorded number of deaths in health-care workers and in the general population based on official reports until Aug 16, 2014.^{1,2} In principle, more recent data could be used for model calibration. The drawback of this approach is that parameter estimate would depend on the simulated effects of all continuing interventions, the effect of which is still uncertain. In the baseline scenario, we set the reporting rates of deaths both in health-care workers and the general population to be 100%. Additionally, to provide an upper bound to our predicted number of cases and deaths, we investigated a second scenario (under-reporting scenario) in which we still assumed 100% reporting in health-care workers but a 50% reporting in the general population-accounting for the possibly raised rate of under-reporting of Ebola virus disease-related deaths. Random-walk Metropolis-Hastings sampling was used to explore the parameter space, checking convergence by using chains of 10000 See Online for appendix iterations (after a 2000 burn-in period) starting from several different initial values of the parameter set. The Markov chain Monte Carlo analysis and the identifiability of parameters are described in the appendix.

Role of the funding source

The funders had no role in study design, data collection and analysis, interpretation, or preparation of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The model calibration yields 830 cases (95% CI 695-969) and 402 deaths (332-478) in Liberia by Aug 16, 2014, assuming perfect reporting of Ebola virus disease cases

	Value	Reference	
Mean duration of incubation period	11·4 days	WHO Ebola Response Team ¹⁵	
Mean time from symptom onset to death	7∙5 days	WHO Ebola Response Team ¹⁵	
Mean time from symptom onset to recovery for survivors	7∙9 days	Gomes et al ^{12*}	
Mean time from symptom onset to hospital admission	5∙0 days	WHO Ebola Response Team ¹⁵	
Proportion of cases admitted to hospital	80%	Gomes et al,12 Khan et al16	
Mean time from hospital admission to death	4∙2 days	WHO Ebola Response Team ¹⁵	
Mean time from hospital admission to recovery for survivors	4∙6 days	Gomes et al12*	
Mean time from hospital admission to dismissal for survivors	11.8 days	WHO Ebola Response Team ¹⁵	
Mean time from death to burial	2∙0 days	Legrand et al14	
Overall case-fatality ratio	54%	WHO Global Alert and Response ²	

Results of sensitivity analyses are shown in the appendix. *Values resulting as the difference between the time from symptom onset or hospital admission to death and time from symptom onset or hospital admission to the end of infectiousness as reported in Gomes and colleagues.¹²

Table 1: Values for the base set of parameters

and deaths (the baseline scenario). If we assume 50% under-reporting in the general population and no underreporting in health-care workers, the model estimates 1571 cases (95% CI 1315-1849) and 805 deaths (672-947) by that date. The actual reporting rate in Liberia is unknown, so these two extreme scenarios are used to cover the uncertainty of the surveillance data. The estimated cases and deaths over time for both of these reporting scenarios are shown in figure 1A. The estimated basic reproduction number (R_o) is 1.84 (95% CI 1.60-2.13) for the baseline scenario and 1.9 (1.62-2.14) for the under-reporting scenario (see table 2 for estimates, and appendix for the calculation procedure). R₀ estimates agree with recent estimates obtained with different mathematical modelling approaches.^{12,15,17-21} In the baseline scenario, we estimated a mean generation time of 18.1 days (SD 12.3). The growth rate of the simulated epidemics is 0.038 per day (95% CI 0.028-0.048), corresponding to a doubling time of 18.6 days (14·3-24·3). In the under-reporting scenario, the generation time is 17.2 days (SD 12.4 days) and the growth rate is 0.043 per day (95% CI 0.031-0.052), corresponding to a doubling time of 16.5 days (13.2-22.4). Such values agree with those reported by the WHO-led team,15 namely a mean estimated generation time of 15.3 days (SD 9.1) and doubling time of 15.8 days (95% CI $14 \cdot 4 - 17 \cdot 4$) in Liberia.

The model was used to estimate the fraction of Ebola virus disease transmission attributable to different settings. As of Aug 16, 2014, under the baseline scenario, we estimate that 52.9% (95% CI 20.3-71.3) of infections occurred in households or in the general community (of which 30.7% [14.1–46.4] were within households), 38.4% (17.4–76.4) in hospitals, and 8.6% (3.2–11.8) at funerals (figure 1B, C; table 2). The estimated household secondary attack rate, or the probability that an infected person will infect a susceptible household member, is 19.4% (95% CI 7.2–34.8), in agreement with values reported in Dowell and colleagues²² for the 1995 outbreak

in the Democratic Republic of the Congo (16%). For the under-reporting scenario, 72% (95% CI 60.2-79.8) of infections occurred in households or in the general community (of which 41.7% [32.9-57.4] were within households), 17.5% (9.3-29.8) in hospitals, and 10.4% $(8 \cdot 8 - 12 \cdot 0)$ at funerals (figure 1B, C; table 2). The household secondary attack rate was estimated to be 36.1% (95% CI 21.8-55.9). The higher estimated household secondary attack rate in the under-reporting scenario stems from the fact that unreported cases can be accounted for only by enhancing transmission in households and the general community, because the finite hospital capacity restricts the number of transmissions occurring in that specific setting. Ebola virus disease transmission attributable to funerals has been estimated by others using case report data to be 9%,15 in good agreement with our transmission modelbased estimates. The lower uncertainty in the estimated values for the under-reporting scenario can be explained by considering that the number of cases in the general population is higher than in the scenario assuming 100% reporting, whereas the number of cases in health-care workers remains the same (figure 1C). This poses an upper constraint on the transmissibility in hospitals.

The calibrated model was used to investigate the features and drivers of the spatial spread of Ebola virus disease in Liberia. Figure 1D, E shows the geographical diffusion of the disease outbreak up to Aug 16, 2014 in the model (see appendix for a full spatiotemporal analysis). Although the model was started with a few localised cases, Ebola virus disease was widespread across most of the country by early August. The spatial drivers of disease spread in our model are contacts across households and infected individuals travelling to hospitals and clinics. We tested different maximum distances between households with frequent contacts from 2.5 km to 20 km, but they had little effect on the model results (appendix). Although this result does not exclude the possible effects from other long-range mobility processes, it does show that up to the initiation of intervention a sufficient driver for the geographical spread of Ebola virus disease is hospitals, where patients infected with Ebola virus and those not infected from a large catchment area can interact. In the appendix we show that the model consistently predicts the week of the first Ebola virus disease case and number of cases over time by county.

The model can be used to provide projections of the future burden of the outbreak, at least in the near future, and to analyse the potential effectiveness of non-pharmaceutical interventions. Figure 2A shows projections for Jan 1, 2015 (18 weeks after the last data used for model calibration), assuming that after early August the available beds in Ebola treatment units increase over time according to data reported by WHO and safe burials are progressively implemented as described in the Methods. In the model calibrated to the

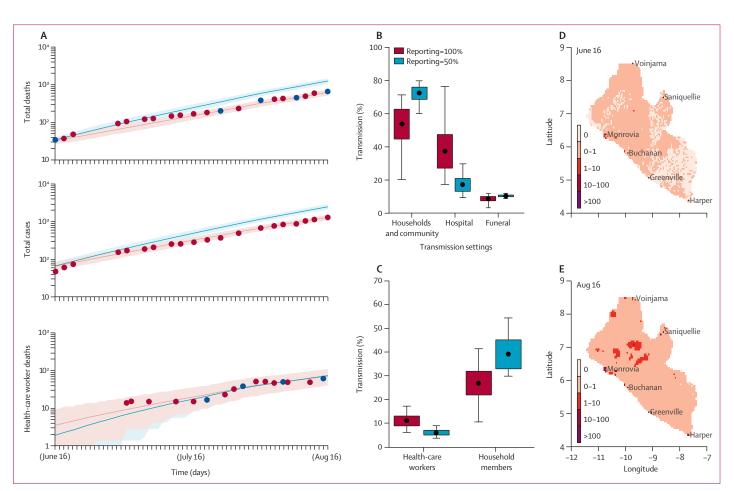


Figure 1: Early spread of Ebola virus disease in Liberia

(A) Top: cumulative number (log scale) of Ebola virus disease deaths over time in the general population of Liberia. Dots refer to the data reported by WHO (blue dots show data used for model initialisation and calibration). Lines and shaded areas refer to estimated mean and 95% CI model predictions, respectively. The scenario that assumes 100% reporting is shown in red, and the 50% under-reporting scenario is shown in blue. The proportion of patients admitted to hospital was assumed to be 80%. Middle: cumulative number (log scale) of Ebola virus disease cases (confirmed, probable, and suspected) over time in the general population; colours as in top. Bottom: cumulative number (log scale) of Ebola virus disease deaths over time in health-care workers; colours as in top. (B) Proportions of infections that occur within households and the community, in hospitals, and during funerals as of Aug 16, 2014. Results that assume 50% and 100% reporting rates in the general population. (D) Simulations of the spatial spread of Ebola virus disease in Liberia as of Jun 16, 2014. Predicted cumulative number of Ebola virus disease cases per cell over time in Liberia, assuming a 100% reporting rate and 80% hospital admission rate. Each cell corresponds to an area of about 25 km². (E) As (D) but as of Aug 16, 2014.

baseline scenario, 11806 cases (95% CI 2387–60856) and 4032 deaths (1085–11446) occurred in the general population and 230 deaths (153–324) occurred in health-care workers by Jan 1, 2015. More cases are projected by the model calibrated assuming 50% under-reporting, with 321127 cases (95% CI 56058–828797) and 34751 deaths (11639–78826) in the general population and 305 deaths (192–426) in health-care workers. The numbers provided by the under-reporting scenario seem hardly compatible with the actual data reported so far in official reports and suggest that under-reporting could not be as high as 50%.

Because of the availability of an increasing number of beds for patients with Ebola virus disease in Ebola treatment units after mid August, in all investigated scenarios hospital transmission drastically decreases over

	100% reporting	50% reporting
β _r (per day)	0.15 (0.04–0.28)	0.37 (0.18-0.65)
β_{h} (per day)	0.33 (0.15-0.67)	0.21 (0.11-0.39)
σ	0.73 (0.27-0.99)	0.56 (0.14-0.98)
Household and community transmission* (%)	52-9 (20-3-71-3)	72.0 (60.2–79.8)
Hospital transmission* (%)	38.4 (17.4–76.4)	17.5 (9.3–29.8)
Funeral transmission* (%)	8.6 (3.2–11.8)	10.4 (8.8–12.0)
R _o	1.84 (1.60–2.13)	1.90 (1.62–2.14)
Household secondary attack rate (%)	19.4 (7.2–34.8)	36.1 (21.8–55.9)

Data are mean (95% CI). *As of Aug 16, 2014. β_i =transmission rate between household members, including their contacts with the deceased during burial ceremonies. β_n =transmission rate in hospitals. σ =scaling factor for the transmission rate in the general community relative to β_i . R_o =reproduction number.

Table 2: Parameter estimates assuming that 80% of cases are admitted to hospital

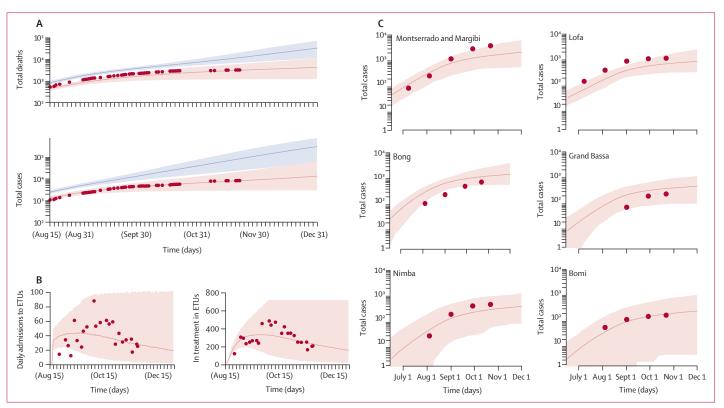


Figure 2: Spatiotemporal dynamics after mid-August, 2014

(A) Number of deaths (top) and cases (bottom) in The general population. Dots refer to the data reported by WHO. Lines and shaded areas are estimated mean and 95% CI model predictions, respectively. Red shows the 100% reporting scenario, blue the 50% reporting scenario. An 80% hospital admission rate was assumed. (B) Left: daily number of admissions to ETUs assuming the 100% reporting scenario. Lines and shaded areas are estimated mean and 95% CI model predictions, respectively. Dots are data reported by WHO. An 80% hospital admission rate was assumed. (B) Left: daily number of admissions to ETUs assuming the 100% reporting scenario. Lines and shaded areas are estimated mean and 95% CI model predictions, respectively. Dots are data reported by WHO. An 80% hospital admission rate was assumed. Right: as left, but for the number of patients infected with Ebola virus receiving treatment in Ebola treatment units. (C) Cumulative number of cases in the general population in the most affected counties of Liberia (the seven counties account for about 97% of overall cases) assuming the 100% reporting scenario. Dots are the data reported by WHO. Lines and shaded areas show the estimated mean and 95% CI model predictions, respectively. ETU=Ebola treatment unit.

	Cases in the population	Mean averted cases
No interventions	36 775 (12 279–107 913)	
Ebola treatment unit only	21 479 (2761–103 295)	15296
Ebola treatment unit and safe burials	11806 (2388–60857)	24969
Ebola treatment unit, safe burials, and protection kits (50% coverage)	6185 (2367-13523)	30590
Ebola treatment unit, safe burials, and protection kits (70% coverage)	5456 (2350–10488)	31319
Ebola treatment unit, safe burials, and protection kits (90% coverage)	4993 (2286-8770)	31782
Data are mean (95% CI) or mean.		

Table 3: Number of projected cases and average number of averted cases as of Jan 1, 2015, assuming 100% reporting and 90% efficacy of household protection kits

time. In particular, as of Jan 1, 2015, the proportion of infection from hospital-based transmission decreases to 17.0% (95% CI 0.9-59.8) and 0.5% (0.1-1.9) in the baseline and under-reporting scenarios. We stress that after mid-August only a negligible number of cases were generated in hospitals because we assume that patients infected with Ebola virus are admitted only to Ebola treatment units. According to WHO estimates, 2373 safe

burials have occurred in Liberia as of Nov 12, 2014, consistent with model estimates, namely 1462 on average (95% CI 310–3293).

Figure 2B shows the number of admissions in Ebola treatment units and the number of patients infected with Ebola virus receiving treatment over time. In agreement with reported data, the model predicts an increase in the number of patients with Ebola virus disease admitted to hospital and who received treatment from mid-August to mid-September and a subsequent decrease. WHO reports after Sept 7, 2014, have shown a decreasing number of cases, suggesting that local chains of transmission have been broken in some districts. This finding is consistent with model simulations characterised by a high proportion of cases generated in hospitals in the initial phase of the outbreak and a consequent later decrease of transmission in hospitals. Although figure 2B shows that more high-quality data to provide field estimates of household secondary attack rate and contact patterns within hospitals and Ebola treatment units are needed to reduce uncertainty of model estimates, the decrease in incidence after September, 2014, is widespread. This finding is very clear

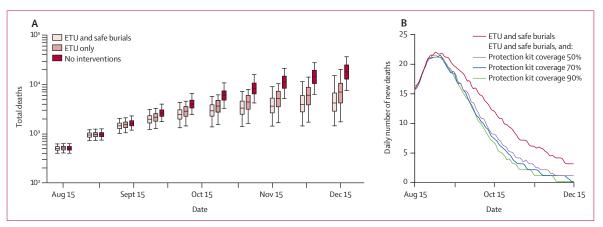


Figure 3: Effect of non-pharmaceutical interventions

(A) Estimated cumulative number of deaths (boxplot shows 2-5%, 25%, 75%, and 97-5% quantiles of the predicted distribution) as predicted by the model by assuming the 100% reporting scenario and considering different degrees of interventions. An 80% hospital admission rate is assumed. (B) Estimated median number of daily deaths by assuming the 100% reporting scenario, the effects of both Ebola treatment units and safe burials, and by varying the coverage of protection kits from 50% to 90%. An 80% hospital admission rate is assumed. ETU=Ebola treatment unit.

in figure 2C, showing that the growth of the cumulative number of cases over time deviates from exponential growth and eventually flattens in all the most affected counties of Liberia.

To quantify the contribution of Ebola treatment unit deployment and safe burials, in table 3 we report the Ebola virus disease cases projected by the model, together with the number of averted cases when compared with a no interventions scenario (figure 3A). In the absence of interventions, the model predicts a total of 36775 cases (95% CI 12279-107913) on Jan 1, 2015 (table 3). We considered the distribution of household protection kits to be a certain proportion of households where a case is identified. According to Centers for Disease Control and Prevention estimates, the protection kit, together with the increased awareness in households where the kit is distributed, could reduce transmission in a household by 90%.13 This situation is modelled by reducing the transmission rate $\beta_{\rm f}$ by 90% (the 50% reduction scenario is analysed in the appendix) for all infectious individuals in the household where the protection kit is supplied, which implies a reduction in the force of infection to which individuals living in both that household and its additional related households are exposed. The same reduction is assumed for funeral transmission.

Since no estimates of the coverage achieved in Liberia are available (hence why we did not include the effects of protection kits in the baseline scenario), we model the effectiveness of deploying protection kits starting from a coverage of 30% of households receiving protection kits up to 90%. The deployment is assumed to increase linearly from 0% on Aug 15, 2014, to the maximum level on Oct 15, 2014 (figure 3B). Deployment of protection kits to about 50% of households might have contributed to further reduce incidence from about 30 daily new cases in November, 2014, to about ten daily cases, a value consistent with WHO reports.

Discussion

The agent-based model presented here can be used for projections of the number of cases and the potential effects of interventions during the current Ebola virus disease outbreak. Early modelling approaches to the epidemic projected a larger number of cases, but they were focusing on the early exponential growth phase of the disease with models that assume the population of Liberia is homogeneous and well mixed.13,15,18 The projections obtained here are closer to the number of Ebola virus disease cases reported by WHO because they take advantage of the population structure and more detailed data for intervention policies. The results show the effect of Ebola treatment units and safe burials in the decrease of incidence seen in Liberia after early September, 2014. Ebola treatment units might have contributed to halving the number of cases and deaths (figure 3A) and safe burial might have contributed an additional 50% reduction compared with a scenario with no intervention. Although quantitative assessment of efficacy and coverage of protection kits is not possible, our results support the hypothesis that the reported decreasing trend of incidence in Liberia might be partly attributable to this mitigation policy. Increasing the coverage of protection kits above the 50% threshold produces marginal improvements with a less than 4% increase in the number of averted cases but a nearly doubling of the effort and cost of deploying protection kits.

Although the presented model is informed by the most recent data available for the Ebola virus disease outbreak in Liberia, data availability is limited, and a number of assumptions should be kept in mind when considering the results of this study. An estimate that is obtained from previous outbreaks is the 80% hospital admission rate. However, even a lower assumed hospital admission rate of 60%, and different assumed transmission models

Panel: Research in context

Systematic review

We queried PubMed and Google Scholar between Aug 1, 2014, and Nov 10, 2014, for manuscripts published in English at any time and containing the following search terms: "Ebola", "EVD", "2014", "Liberia", "transmission models", "agent based models", and "interventions". Legrand and colleagues¹⁴ introduce a homogeneous mixing model accounting for the main routes of Ebola virus transmission, namely community, hospitals, and funerals. Models with similar epidemiological structure have been developed to provide estimates for the continuing Ebola virus disease epidemic in west Africa,^{91.013} and for the prediction of the international spread.^{11.12} Models with a simplified compartmental structure have been used to estimate the reproduction number of the epidemic.¹⁷⁻²⁰ Here, we aim to improve estimates by explicitly accounting also for transmission in households and spatial structure of the population, an approach similar to that previously used to study the spread of other infectious diseases (eg, influenza).³⁻⁸ We rely on official Liberian Ministry of Health and WHO reports¹² for the epidemic data and the report by the WHO Ebola Response Team¹⁵ for the disease natural history parameters.

Interpretation

This is the first study based on a microsimulation approach to assess the relative importance of different settings relevant to Ebola virus disease transmission and the spatial dynamics of the epidemic. The approach allows a thorough assessment of the effectiveness of intervention options. However, our study emphasises that, in view of the uncertainty of model estimates, high-quality data (eg, quantitative estimates of household secondary attack rate, contact patterns within hospitals, and effects of the continuing interventions) are needed to improve model estimates. The model could be used to assess strategies and effectiveness of pharmaceutical interventions such as vaccines when data become available.

in hospitals, do not change the results substantially (appendix). Model estimates also do not vary substantially when the case-fatality ratio is increased to 70.8%, according to more recent, but highly variable, estimates¹⁵ (appendix), and by assuming key natural history parameters derived from the analysis of previous outbreaks12,14 (appendix). Our results also suggest that the reporting rate is probably much greater than 50%. However, the uncertainty of model estimates and sensitivity of results to assumptions about the reporting rate call for urgent field estimates of the reporting rate, because it is probably lower than 100%. Uncertainty of model estimates and sensitivity of results to the values of the transmission rates in households and hospitals (figure 1B) show that more high-quality data to provide field estimates of the household secondary attack rate and contact patterns within hospitals are needed to reduce uncertainty of model estimates. Finally, model estimates would benefit from quantitative estimates of efficacy of the continuing interventions, especially for protection kits (panel). Moreover, it would also be key to inform the model with detailed estimates of practical implementation of policies, because simply providing supplies of equipment might not be sufficient.23

We assume that each infectious individual can transmit the infection in the general community on a daily basis to a restricted number of individuals (corresponding to two additional households, in the reference scenario) living inside a circle (of 10 km radius, in the reference scenario) around the household of each patient with Ebola virus disease. This choice derives from the fact that no evidence of pre-symptomatic Ebola virus disease transmission has been reported so far. Thus, infectious individuals with Ebola virus disease would be very unlikely to be in a condition to travel long distances, except for those urgently needing hospital care. Susceptible individuals coming into contact with patients with Ebola virus disease would mainly be visiting relatives and friends. The reliability of such hypotheses is supported by our analysis, presented in the appendix, showing that even a model accounting for Ebola virus disease transmission in the community only at 2.5 km at most is able to reproduce the recorded pattern of spatial spread, and our projections are fairly insensitive to such an extreme assumption. Our findings are also robust with respect to increasing the number of contacts in the general community (here modelled as additional households in the network of daily contacts of each individual) and to the distance at which contacts are made (appendix). Therefore, although we cannot rule out that local population mobility could represent a possible driver of Ebola virus disease dynamics in the future, for the moment no evidence exists that such mobility is necessary to explain what has been reported so far. However, we warn that we do not explicitly consider mobility due to commuting patterns or other business travel. Although this kind of mobility is not likely to play a very important part in Ebola virus transmissionmobile people are generally not symptomatic and thus have near zero or very low infectivity-we cannot exclude their relevance in increasing the geographical dispersion of the outbreak.

This modelling approach can be extended to other countries in west Africa and include more detailed policies for the isolation of cases, Ebola treatment unit management, and funeral preparation. We did not investigate pharmaceutical interventions such as vaccines because data on their efficacy are not available. However, the model could be used to analyse the potential effectiveness of these interventions and their deployment strategies as data become available.

Contributors

SM, MA, LF, MFCG, APyP, DLC, and AV provided the data. SM, MA, and LF did the computational experiments. SM and AV conceived the study. All authors analysed the data, discussed the results, edited, and commented on the draft report. All authors read and approved the final manuscript.

Declaration of interests

We declare no competing interests.

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