Transmission dynamics of Ebola virus disease and intervention effectiveness in Sierra Leone

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Sierra Leone is the most severely affected country by an unprecedented outbreak of Ebola virus disease (EVD) in West Africa. Although successfully contained, the transmission dynamics of EVD and the impact of interventions in the country remain unclear. We established a database of confirmed and suspected EVD cases from May 2014 to September 2015 in Sierra Leone and mapped the spatiotemporal distribution of cases at the chiefdom level. A Poisson transmission model revealed that the transmissibility at the chiefdom level, estimated as the average number of secondary infections caused by a patient per week, was reduced by 43% [95% confidence interval (CI): 30%, 52%] after October 2014, when the strategic plan of the United Nations Mission for Emergency Ebola Response was initiated, and by 65% (95% CI: 57%, 71%) after the end of December 2014, when 100% case isolation and safe burials were essentially achieved, both compared with before October 2014. Population density, proximity to Ebola treatment centers, cropland coverage, and atmospheric temperature were associated with EVD transmission. The household secondary attack rate (SAR) was estimated to be 0.059 (95% CI: 0.050, 0.070) for the overall outbreak. The household SAR was reduced by 82%, from 0.093 to 0.017, after the nationwide campaign to achieve 100% case isolation and safe burials had been conducted. This study provides a complete overview of the transmission dynamics of the 2014–2015 EVD outbreak in Sierra Leone at both chiefdom and household levels. The interventions implemented in Sierra Leone seem effective in containing the epidemic, particularly in interrupting household transmission.

Ebola virus disease | spatiotemporal modeling | household transmission | secondary attack rate | intervention effectiveness

The unprecedented outbreak of Ebola virus disease (EVD) in West Africa during 2013–2015 led to 28,638 confirmed, probable, and suspected cases, with 11,316 deaths as of 20 January 2016 (1). In Sierra Leone, the first EVD case was confirmed on 25 May 2014, and further investigations identified a total of 14 cases, all of whom had attended the burial of a traditional healer who had contacted and provided treatment to EVD patients from Guinea. The disease spread rapidly in the Eastern Province of Sierra Leone adjacent to the epicenter of the outbreak in Guinea (2, 3). Freetown, the capital of Sierra Leone, identified its first imported case on 11 July 2014, when over 300 confirmed cases with 99 deaths had been reported throughout the country (tomfernandez28.com/2014/07/14/ebola-spreads-to-sierra-leone-capital-of-freetown-as-deaths-rise, accessed 30 January 2016). To contain the rapid dissemination of the disease, the Sierra Leonean government declared a State of Emergency on 6 August 2014 and dispatched military personnel to enforce quarantines in areas with intense transmission, followed by a 3-d nationwide quarantine 19–21 September 2014. About 28,500 trained community workers and volunteers went door-to-door to promote infection prevention (4). As part of the strategic plan of the United Nations Mission for Emergency Ebola Response (UNMEER), Sierra Leone initiated a campaign in early October 2014 to isolate all reported EVD cases by active case finding and contact tracing, and to perform safe and dignified burials for all EVD-related deaths. The country worked with its international partners to establish healthcare facilities and diagnostic laboratories, and to promote social mobilization and community engagement (5). About 1.5 y after occurrence of the first EVD case, the World Health Organization (WHO) on 7 November 2015 declared that Ebola virus (EBOV) transmission had been stopped in Sierra Leone and verified 8,704 confirmed infections, with 3,589 deaths; however, a new case was identified on 14 January 2016 (1, 6).

Since the first recognized EVD outbreak in 1976, a total of 25 outbreaks have been reported around the world. The growing concern over the repeated emergence of EVD (7, 8) has stimulated many studies on these outbreaks, in particular on the most recent one in West Africa, trying to understand the transmission mechanisms and the effectiveness of containment strategies (9–18). These studies, however, either used limited data at an early stage of the epidemic or assessed a single influential factor. Only a few

Significance

Since the initial recognition of Ebola virus disease (EVD) in 1976, many epidemics have occurred in Africa. Serious concerns remain that the fatal disease may repeatedly reemerge. In this study, we used data from an unprecedented EVD outbreak in Sierra Leone to map spatiotemporal transmission patterns, identify influential factors, and assess the effects of interventions at the chiefdom level. Furthermore, we have quantified household transmissibility and the temporal association between interventions and household transmission. Our findings have deepened the understanding of the transmission dynamics of EVD and provided key information for future modeling efforts in forecasting future epidemics and establishing intervention strategies.

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studies have attempted to capture the spatial component in the epidemic data (18, 19). In addition, efforts to quantify the transmissibility of EVD in households, an important transmission venue for many contagious diseases, have been hindered by lack of data.

In this study, by integrating a comprehensive dataset of EBOV-testing records of persons under investigation (PUIs) reported to the Sierra Leone Ministry of Health and Sanitation (SLMHS), we mapped and analyzed spatiotemporal transmission dynamics of EVD at the chiefdom level in Sierra Leone, identified socioenvironmental factors contributing to the risk of transmission, and assessed the effects of interventions in different epidemic phases. We also identified patients living in the same household, based on case investigation forms, and assessed household transmissibility of EVD and the effects of interventions on household transmission.

Results

Essential data of 8,358 confirmed and 3,545 suspected EVD cases were extracted from a total of 95,089 EBOV-testing records of PUIs reported to the SLMHS from May 2014 to September 2015. Based on symptom onset dates, epidemic curves were created by plotting the daily number of confirmed and suspected cases (Fig. 1). After 3 mo of the epidemic persisting at a relatively low level, the number of confirmed cases soared beginning in mid-August 2014, peaked in early November 2014, and then declined gradually but consistently despite some fluctuation. The time points of intervention events are shown by using arrows along with the epidemic curves (Fig. 1). The epidemic started to decline a few weeks after the initiation of the nationwide campaign of case isolation and safe burials in early October 2014. After the 1-mo "Zero-Ebola" campaign initiated in mid-March 2015, only a few cases were confirmed each day. No confirmed case has occurred since 6 September 2015. The epidemic curve of confirmed and suspected cases combined was similar to that of confirmed cases although the proportion of suspected cases increased over time (*SI Appendix*, Fig. S1). A total of 307 healthcare workers were confirmed to be infected. The proportion of healthcare workers among confirmed cases was quite high from June to August 2014 and was dramatically reduced after September 2014 although a considerable number of healthcare workers were still infected up to January 2015 (*SI Appendix*, Fig. S2).

One hundred fourteen of 150 chiefdoms in Sierra Leone were affected during the outbreak (Fig. 1). The more densely populated chiefdoms seemed to have more confirmed cases (Fig. 2*A*). The spatial distribution of EVD in each month varied greatly (*SI Appendix*, Fig. S3), and the cumulative incidence rates among chiefdoms were notably heterogeneous across the country (Fig. 2*B*). A trend surface analysis revealed two spatial diffusion corridors of EVD. One originated on 18 May 2014 from the border area of Kailahun District in the east adjacent to the EVD epicenter in Guinea. The other began on 25 June 2014 from Western Urban and Rural Districts in the west. Both rapidly spread toward Tonkolili and Bo districts of central Sierra Leone and subsequently diffused northeast and southwest with a reduced velocity (Fig. 2*C*). Most of the spatial diffusion process was accomplished within about 120 d after the occurrence of the first case. To assess the association between invasion of EVD and socioenvironmental factors, we performed a survival analysis of the time delay of the first confirmed case in affected chiefdoms after 18 May 2014, the onset date of the first confirmed case in the country, where unaffected chiefdoms were considered as right-censored. Intersection with primary and secondary roads increased the hazard of invasion by 50% and 65%. The hazard was increased by about 29% per 10-km decrease in distance between a chiefdom and its nearest hospital (*SI Appendix*, Table S1). When both confirmed and suspected cases were included in the model for sensitivity analyses, similar results were obtained, after adjusting for population density (*SI Appendix*, Table S2). These significant factors for EVD invasion were then overlapped on the land cover map of Sierra Leone (Fig. 2*D*).

Using a weighted-average linkage-clustering method (20), we grouped the 114 affected chiefdoms into six categories of epidemic patterns. Pattern I included 31 chiefdoms with only sporadic cases. Pattern II included 16 chiefdoms where several cases occurred within a period of 2 or 3 wk. Pattern III included 27 chiefdoms where there was a small-scale outbreak in a short period. Pattern IV included 24 chiefdoms with either multiple small-scale outbreaks or a continuous low-level epidemic over a long period. Pattern V included 11 chiefdoms where a continuous medium-scale outbreak was observed. Pattern VI included five chiefdoms with a prolonged outbreak over a quite long period (Fig. 3*A* and *SI Appendix*, Fig. S4). Generally, a category with a higher number indicates a more sustained epidemic in the chiefdom. Chiefdoms with pattern IV, V, or VI were mainly in the western and central regions (Fig. 3*B*) and had both larger population sizes and higher population densities (*SI Appendix*, Table S3).

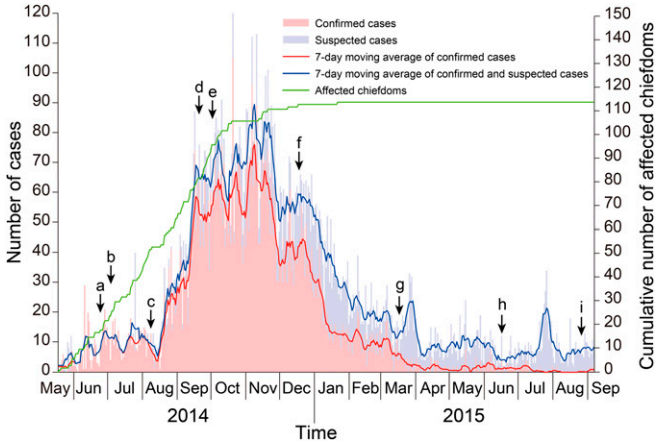

Fig. 1. The epidemic curves of Ebola virus disease (EVD) based on the dates of symptom onset for confirmed and suspected cases in Sierra Leone from May 2014 to September 2015. The dates of key events in relation to interventions of EVD in Sierra Leone are indicated by black arrows: (arrow a) Opening of the first Ebola treatment center in Kenema District on 24 June 2014; (arrow b) establishment of the first diagnostic laboratory in Kenema District on 2 July 2014; (arrow c) declaration of the national state of emergency on 6 August 2014; (arrow d) a 3-d nationwide quarantine from 19 to 21 September 2014; (arrow e) initiation of the United Nations Mission for Emergency Ebola Response strategic plan on 1 October 2014; (arrow f) operation of "Western Area Surge" on 17 December 2014; (arrow g) initiation of a 1-mo "Zero-Ebola" campaign in mid-March of 2015; (arrow h) beginning of "Operation Northern Push" on 16 June 2015; and (arrow i) initiation of ring vaccination in late August of 2015.

We developed a Poisson model that simultaneously accounted for three transmission routes: importation of cases from any non-neighboring chiefdoms, transmission within chiefdoms, and transmission from neighboring chiefdoms. This model explained a substantial amount of the spatiotemporal variation in the case numbers (*SI Appendix*, Fig. S5 and Table S4). The average number of infections in any chiefdom imported per week from non-neighboring chiefdoms was estimated as 0.035 (95% CI: 0.022, 0.050). The average number of secondary cases infected by an infective patient per week in the same chiefdom was estimated to be 0.84 (95% CI: 0.64, 1.07). The transmission rate from neighboring chiefdoms was only 2.7% (95% CI: 1.8%, 3.7%) of that within the chiefdom (*SI Appendix*, Table S5). Compared with the reference phase before October 2014 when the strategic plan of UNMEER was initiated, person-to-person transmissibility, estimated as the average number of secondary infections caused by a patient per week, was reduced by 43% (95% CI: 30%, 52%) during October–December 2014, when case isolation and safe burials were quickly promoted to essentially achieve 100% (intervention phase I) and by 65% (95% CI: 57%, 71%) thereafter (intervention phase II). In comparison with the incidence rate in the ethnic group Mende, the incidence rates in other ethnic groups were 40–50% higher. In general, transmission risk was associated with high population density, proximity to Ebola treatment centers (ETCs), and high coverage of cropland (Fig. 4 *A*–*C*). The effect of temperature was nonmonotonic. The transmission risk reached its minimum at an atmospheric temperature of 27.1 °C but increased

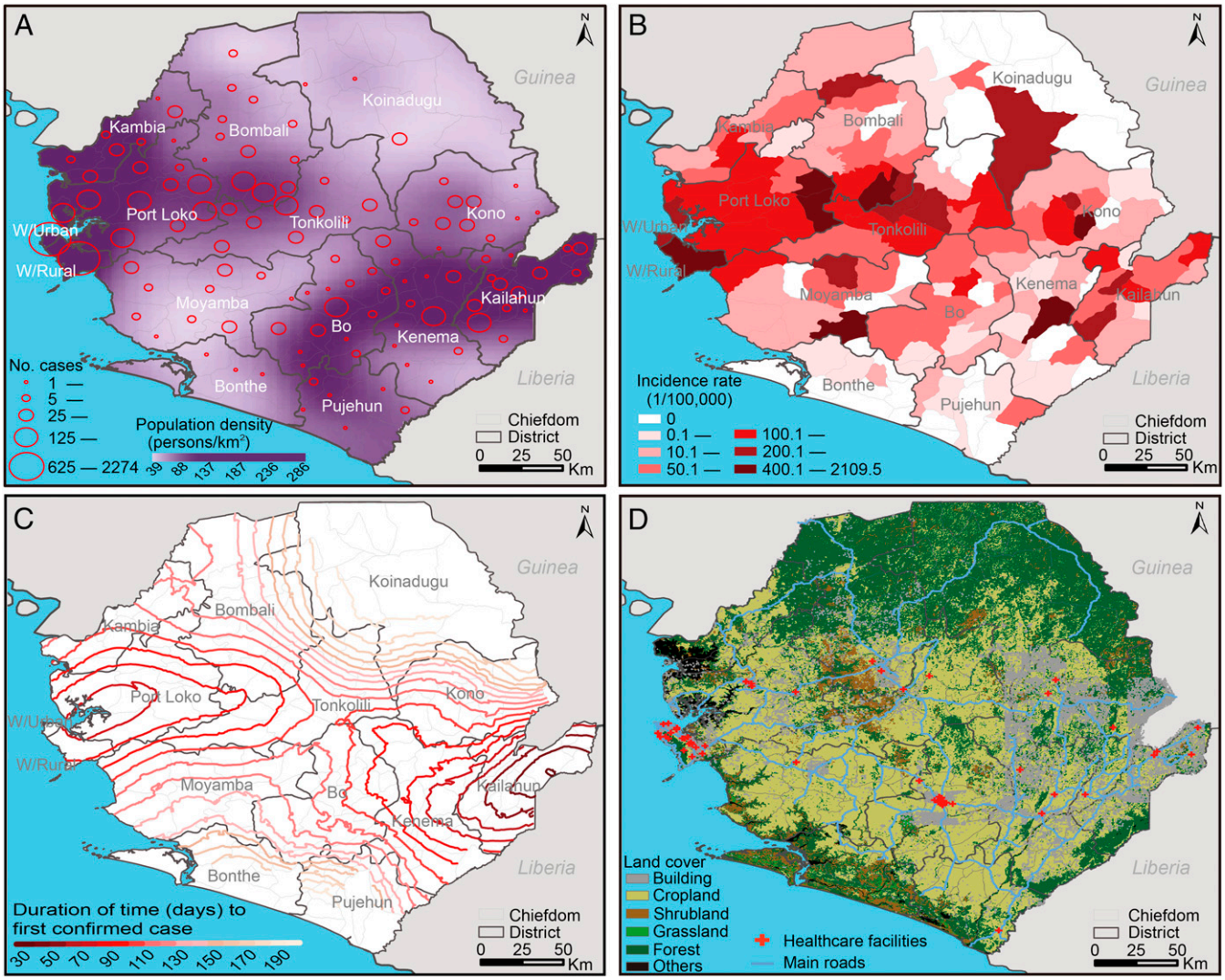

Fig. 2. The spatial distribution and spread trend of Ebola virus disease (EVD) in Sierra Leone from May 2014 to September 2015. (*A*) Total number of confirmed cases in each chiefdom with the background of population density. (*B*) Cumulative incidence rate of confirmed cases in each chiefdom. (*C*) The spatial trend contour of EVD spread in Sierra Leone. The EVD spread from areas in dark red to areas in light red, and a wider gap between contours indicates a quicker diffusion velocity. (*D*) A land cover map of Sierra Leone overlapped with the major transportation network and healthcare facilities.

when the temperature was either lower or higher (Fig. 4*D*). The ranges of bootstrap risk ratio curves are relatively wide at their two ends, indicating uncertainty at the extreme values of these variables where observations are often sparse. Relative humidity was not included in our primary analysis due to its high correlation with temperature. A further analysis including relative humidity as a covariate neither improved the fit of the model to the data nor changed the effects of other variables (*SI Appendix*, Fig. S6 and Table S6). When both confirmed and suspected cases were included in the model, the results were essentially similar, except that the intervention effects were smaller, with reduction rates of 31% and 47% for intervention phase I and II, respectively (*SI Appendix*, Fig. S7 and Table S7).

By linking laboratory-tested EVD cases using self-reported names of household heads, contacts with EVD symptoms (referred to as source contacts), and residential addresses, we identified 1,554 individuals potentially from 634 households, each with at least two members. Under the assumption that self-reported source contacts were all infected by EBOV, the estimates of the secondary attack rate (SAR), defined as the probability that an index patient infects a household contact within his or her infectious period, ranged from 0.056 to 0.062 for nine combinations of possible distributions of the incubation and infectious periods (Fig. 5*A*). Assuming a mean incubation period of 10 d and a mean infectious duration of 11 d, the estimated SAR was 0.059 (95% CI: 0.050, 0.070). Males tended to be less prone to household infection than females, with an odds ratio of 0.62 (95% CI: 0.44, 0.88) (Fig. 5*B*). The odds ratio between children and adults was 1.36 (95% CI: 0.95, 1.97), suggesting that children were likely more prone to household infection, although not statistically significant (Fig. 5*C*). The SAR among female children was estimated as 0.11 (95% CI: 0.063, 0.18). Neither age nor gender was found to impact infectiousness (*SI Appendix*, Fig. S8 *A* and *B*). The sensitivity analyses assuming that all individuals with symptom onsets were infected showed comparable results (Fig. 5 *D*–*F* and *SI Appendix*, Fig. S8 *C* and *D*).

To explore the effect of nationwide interventions on household transmissibility, we then estimated the SAR on or before 22 October 2014 and that after. This time point was the date when the nationwide campaign to achieve 100% case isolation and safe burial had been ongoing for 3 wk (the longest incubation period of EVD). Under the same assumptions about the incubation and infectious period as in the primary analysis, we estimated the SAR to be 0.093 (95% CI: 0.077, 0.11) before 22 October 2014 and 0.017 (95% CI: 0.0095, 0.031) after. The corresponding estimates for the household-specific reproductive number are 0.46 and 0.085,

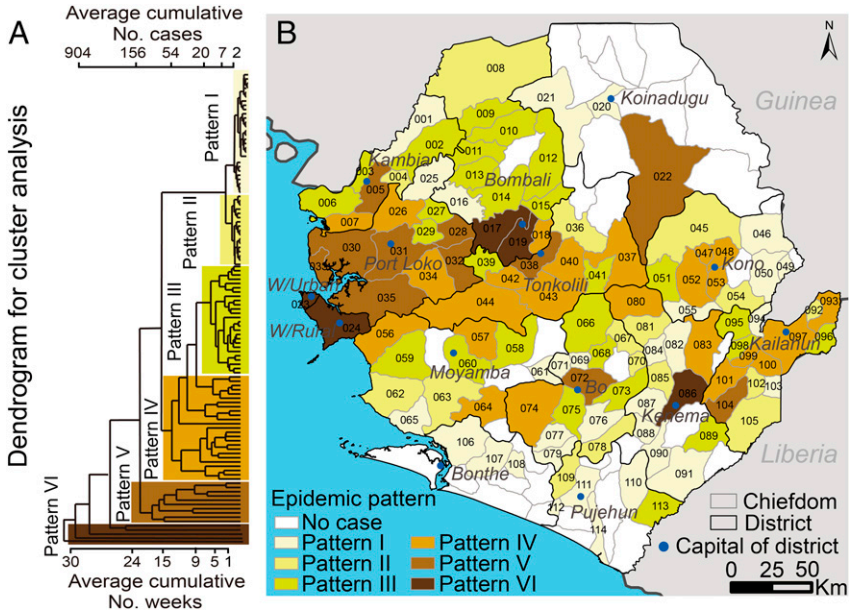

Fig. 3. Chiefdom-level epidemic patterns of Ebola virus disease in Sierra Leone. (*A*) Dendrogram based on the clustering analysis, classifying chiefdom-level epidemics into six patterns. (*B*) Map showing the spatial distribution of the epidemic pattern of each affected chiefdom. The identification number of each affected chiefdom is indicated in the map. The identification number of each chiefdom is listed in *SI Appendix*, Table S11.

respectively, taking into account the average household size in Sierra Leone. The reduction of about 82% in the household SAR might be attributable to the intensification of intervention programs during the last quarter of 2014 (*SI Appendix*, Table S8). This finding was robust to variation in the assumptions about the incubation and infectious periods.

Discussion

This study provides a complete overview of the transmission dynamics of the 2014–2015 EVD outbreak in Sierra Leone at both the chiefdom and household levels. Our primary analysis was based on confirmed cases and their symptom onset dates. When both suspected and confirmed cases were used for sensitivity analyses, the overall results were consistent although the proportion of suspected cases increased over time, especially in the late phases of the epidemic. The increased relative frequency of suspected cases was most likely due to enhanced case finding and contact tracing, which subsequently brought in more patients with EVD-like symptoms who might have been infected with other pathogens.

The EVD epidemic affected 114 of 150 chiefdoms in Sierra Leone and presented obvious spatial heterogeneity in cumulative incidence rates across the country (Fig. 2*B*). Invasion of EVD into a chiefdom was significantly associated with being intersected by primary and secondary roads, which are vital connections between rural towns and densely populated cities (21). This association may be because convenient access to the roads facilitated transportation of EVD patients or dead bodies and therefore contributed to the rapid and extensive spread of the disease in Sierra Leone. In contrast, the simultaneous EVD outbreak in the Democratic Republic of Congo of Equatorial Africa is much smaller because it occurred in remote forested areas, where human contacts were limited due to small populations and infrequent connections by poor communication and transportation (22). The association between the invasion of EVD and proximity to the transportation network might have been due to enhanced surveillance capacity because the transportation network provided easier access to diagnostic and healthcare facilities.

The proximity to hospitals was found to be associated with a higher hazard of invasion of chiefdoms by EVD. This association might have been partially due to surveillance bias: i.e., cases near hospitals were more likely to be diagnosed and reported. On the other hand, nosocomial transmission potentially played a role in the geographical expansion of EVD (14, 23, 24). The proportion of healthcare workers among all confirmed cases was relatively high in June–August 2014 (*SI Appendix*, Fig. S2). Patients who had EVD-like symptoms caused by other pathogens and visited hospitals with EBOV-infected cases were also at high risk of infection (24). In addition, chiefdoms with sustained outbreaks (patterns IV, V, and VI) were mainly found in densely populated regions where main roads and hospitals cluster (Figs. 2*D* and 3*B*), supporting the contribution of nosocomial transmission. A sufficient supply of personal protective equipment (PPE) and timely training of medical staff may help curb nosocomial transmission in future outbreaks.

Our analyses showed a temporal association between implementation of multiple interventions and control of the epidemic. The control efforts, in particular the establishment and operation of diagnostic and healthcare facilities as well as the national and regional campaigns to improve case isolation and safe burial, were accumulating quickly during the last quarter of 2014 and achieved the final goal in January 2015. These multilayer interventions were

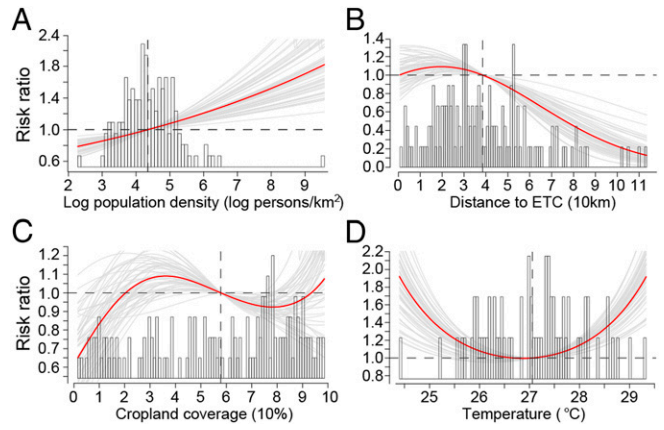

Fig. 4. Association between estimated risk ratios (RRs) and socioenvironmental factors. The RRs are estimated based on the Poisson transmission model and are plotted as a function of (*A*) population density, (*B*) distance to the nearest Ebola treatment center (ETC), (*C*) cropland coverage, and (*D*) weekly average atmospheric temperature. Estimated RR curves are in red. Uncertainty is shown by estimated curves (in gray) based on 50 (randomly selected from 1,000) bootstrap samples of the dataset. The histograms represent the distribution of the socioenvironmental factors. The cross points of horizontal and vertical dash lines indicate the mean values of the socioenvironmental factors at which the RR is 1.

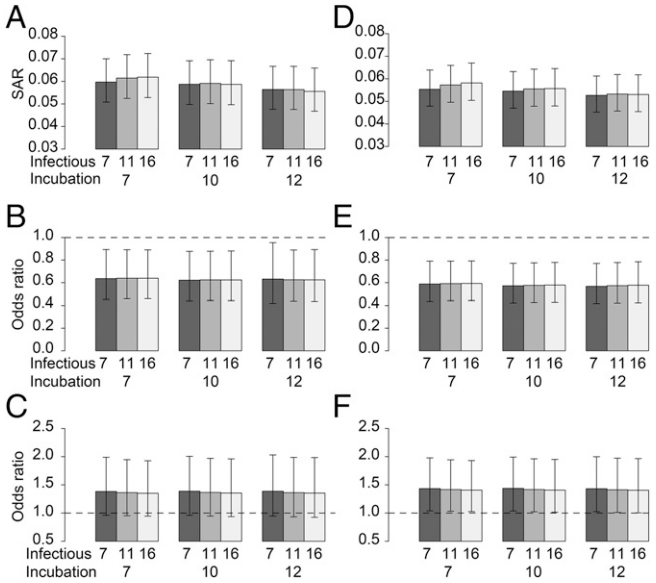

Fig. 5. Estimates for household secondary attack rate (*A* and *D*) and effects of gender (*B* and *E*, odds ratio between males and females) and age group (*C* and *F*, odds ratio between children and adults) on susceptibility, stratified by mean durations of the incubation and infectious periods. The estimation was also stratified by either confirmed cases (A–C) or clinical cases (with symptoms but not necessarily confirmed) (D–F). Presented in *A* and *D* are estimates for the overall secondary attack rate without adjusting for age, gender, or epidemic phase.

associated with a 43% reduction in population-level transmission risk during intervention phase I and a 65% reduction during intervention phase II. Due to the lack of data about the implementation of interventions in individual chiefdoms, we were unable to differentiate the effects of each kind of intervention. The number of beds in healthcare facilities has been used as a surrogate for the intervention intensity (18). The number of beds was closely related to, but may not fully capture, the overall intervention intensity. The epidemic started to recede in late November 2014 when the number of beds met half of the needs but the number of burial teams had almost reached the needed level (*SI Appendix*, Table S8). The difference in incidence rates among ethnic groups might be due to their geographic locations, economic development, social behaviors, or religious traditions. Further investigations are needed to elucidate this issue.

Using real-time data from a weather station in Freetown, we found the temporal trend of the epidemic was correlated with the variation in atmospheric temperature. This finding is consistent with a previous study that used historic climatic data (25). It is interesting to note that, although the range of temperatures in Sierra Leone is relatively narrow (24–30 °C), either low or high (relative to the mean) temperatures were associated with increased risks by up to 80% (Fig. 4*D*). The fact that low monthly average temperature was remarkably correlated with high monthly average rainfall implies a possible role of the peak rainy season from July to September in Sierra Leone (*SI Appendix*, Fig. S9), although rainfall was not included in the analysis because it was not available. Ebola virus is an enveloped virus, which makes it quite susceptible to degradation in high temperature environments. It is unclear why high temperatures were associated with increased transmission risk in this study. One possibility is that high temperatures could increase the exposure of contacts to EVD patients due to sweating or less clothing.

We provide, to our knowledge, the first quantification of household transmissibility for EVD in the West Africa outbreak. Our SAR estimate for the early stage of the epidemic, 0.093, was similar to 0.05–0.09 for the outbreaks that occurred in Zaire in 1976 and in the Republic of Congo in 2005 (26, 27), but much lower than 0.16–0.22 for the outbreaks in southern Sudan in 1979 (28) and in Kikwit of Congo in 1995 (29). These higher estimates could be overestimates because they did not take into account community sources or tertiary transmission within families, and the outbreaks were likely selected due to the substantial number of secondary cases. On the other hand, our analysis could be subject to underestimation of the SAR because some cases from the same households might not be identified or confirmed. In addition, potential bias could result from the difference in the size distribution between infected households and general households in the country. A retrospective household study to verify our findings would be helpful. A contact-tracing study in Conakry, Guinea in 2014 found that 72% of transmission occurred among family members (30). Contact-tracing studies may also be able to quantify transmissibility in additional settings, such as hospitals and funerals (31, 32).

Females tended to be more likely to be infected within households than males, possibly due to their role as care givers for EVD, consistent with previous findings (29). In contrast to historic belief, children seemed more prone to household infection than adults in this study. The proportion of children was 26% among confirmed cases in the identified households, similar to 25% children among all confirmed cases in Sierra Leone. The possibility of an excessive number of confirmed children cases in household data can thus be considered unlikely.

A phase III Ebola vaccine efficacy (VE) trial based on contact tracing in Guinea has shown a high efficacy (33), and the use of this vaccine has also started in Sierra Leone (1). We suggest that future vaccination trials or campaigns be accompanied by carefully designed household, contact-tracing cluster, hospital, or community transmission studies, so that various aspects of VE can be measured: e.g., the VEs in reducing susceptibility, infectiousness, and pathogenicity (34). Plans could be made now, using the methods presented here, to help with the conduct and analysis of such vaccine trials, as well as with assessing the effectiveness of vaccination control strategies.

Materials and Methods

Data Collection and Management. We collected all EBOV-testing records of PUIs reported to SLMHS from May 2014 to September 2015 and established a database including information on individual identification number, name, age, gender, residential address, date of symptom onset, date of specimen collection, date of specimen testing, and interpretation of EBOV-testing result. Confirmed or suspected cases were defined according to the diagnostic criteria developed by the WHO (35). We then removed duplicated records of confirmed and suspected cases. A few confirmed and suspected cases without sufficient information for duplicate checking were excluded from the database. If additional samples of suspected cases tested positive for EBOV, they were then considered as confirmed cases and excluded from the list of suspected cases. Data regarding EBOV infection of healthcare workers were collected to explore nosocomial transmission. Another dataset of PUIs, whose samples were tested from August to December 2014, was used to estimate the household transmissibility. Additional information on household head, clinical manifestations, and contact history was collected using a standardized WHO case investigation form. We also obtained data on chiefdom boundaries, population and housing census, building distribution, land cover, transportation, locations of hospitals and ETCs, poverty level, and ethnic groups for each chiefdom (*SI Appendix, Supplementary Materials and Methods*, sections 2 and 3). Chiefdom is the third-level administrative unit in Sierra Leone, below province and district. There are four provinces (areas), 14 districts, and 153 chiefdoms. The four chiefdoms within Western Rural District have been combined in our chiefdom-level analyses due to their small scope, leaving 150 chiefdoms for our chiefdom-level analyses (Dataset S1).

Temporal and Spatial Analyses. Epidemic curves were created by plotting the daily number of newly confirmed and suspected cases. Each confirmed case was georeferenced and linked to a digital map of Sierra Leone (downloaded from www.gadm.org) according to the chiefdom where onset occurred using Geographic Information System (GIS) technologies (Dataset S2). The thematic map was created by displaying the cumulative number of confirmed EVD cases in each of the affected chiefdoms. A spatial trend contour plot of the EVD spread was developed using a trend surface analysis (36, 37). The time between adjacent contours was fixed at 20 d, and a longer distance between adjacent contours indicates a faster spatial diffusion of the disease. Chiefdom-specific temporal patterns of EVD were presented as heat maps of weekly numbers of cases over the epidemic period (38, 39). We further grouped the chiefdoms into six categories according to their epidemic characteristics by

using a weighted-average linkage method (20), which was linked to the heat map (*SI Appendix, Supplementary Materials and Methods*, section 4). Survival analysis was performed to explore the factors associated with the spatial diffusion of EVD across chiefdoms, and univariate and multivariate Cox proportional hazard models were fitted to the chiefdom-level invasion times, where unaffected chiefdoms were considered right-censored (*SI Appendix, Supplementary Materials and Methods*, section 5).

Poisson Transmission Model. A Poisson transmission model was developed to account for both case importation and local transmission, adjusting for the following socioenvironmental factors: population density; weekly average temperature and relative humidity with a 2-wk lag; distances to nearest primary roads, secondary roads, or railroads; distances to the nearest hospital and ETC; coverage percentages of cropland, forest, and shrub; poverty level; intervention phase; and primary ethnic groups. One particular purpose of this model was to assess the effectiveness of the intervention programs implemented in Sierra Leone (*SI Appendix, Supplementary Materials and Methods*, section 6) via examining potential temporal variation of the transmission rate across intervention phases. The definition of intervention phases was based on the time frame of the UNMEER-coordinated efforts to achieve 100% case isolation and 100% safe burials, which covered October–December 2014. Because the epidemic was modeled on the basis of calendar weeks (counting from Monday, 30 December 2013), we defined the period of 29 September–28 December 2014 (calendar weeks 40–52) as intervention phase I. The weeks before 29 September and the weeks after 28 December 2014 were defined as the reference phase and intervention phase II, respectively. Variances of the estimates were obtained using the bootstrap. To ensure identifiability, we considered only up to cubic terms for each factor. Major interventions and events are summarized in *SI Appendix*, Table S8 and *Supplementary Materials and Methods*, section 6. Technical details including the formulae of the model and data inclusion and exclusion criteria are given in *SI Appendix, Supplementary Materials and Methods*, section 7.

Household Transmissibility. A household in the analysis of household transmissibility of EVD was defined as a group of related family members who live at the same street address and therefore are likely to have daily close contact with each other. Based on the individual data from the standardized WHO case investigation form, possible households were identified by matching individuals who were from the same district and provided the same names (encrypted) of household heads and street addresses (encrypted). We assessed household transmissibility using a chain-binomial transmission model with a built-in expectation-maximization algorithm to account for uncertainty in infection status of some household members (*SI Appendix, Supplementary Materials and Methods*, section 8). According to the current knowledge about the natural history of EVD (40), we defined three probability distributions for the incubation period (means: 7, 10, and 12 d) on the range of 1–21 d and three probability distributions for the infectious period (means: 7, 11, and 16 d) on the range of 1–30 d. We performed sensitivity analyses based on the nine combinations of the distributions. This model was coupled with multiple imputation of household sizes based on the 2004 census data of Sierra Leone (*SI Appendix*, Tables S9 and S10) and of missing age and gender based on the observed household data. Each susceptible individual was assumed exposed to both the community at large and infectious household members. The SARs and the effects of covariates, such as age group and gender, were assessed via logistic regression. Technical details about the household data, the model, assumptions of natural history of EVD, handling of missing data, and covariate adjustment are given in *SI Appendix, Supplementary Materials and Methods*, section 8.

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