

Regional Spread of Ebola Virus, West Africa, 2014

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To explain the spread of the 2014 Ebola epidemic in West Africa, and thus help with response planning, we analyzed publicly available data. We found that the risk for infection in an area can be predicted by case counts, population data, and distances between affected and nonaffected areas.

The first cases of the 2014 Ebola epidemic in West Africa (49 cases in Guinea) were reported on March 21 (1). By November 4, the World Health Organization had reported 13,241 cases in the 3 primarily stricken countries of Guinea, Sierra Leone, and Liberia and single cases in Senegal and Mali (2). Although virus transmission to other countries (Nigeria, United States, and Spain) has occurred via air travel, most infections have spread regionally via ground movement of sick persons. To aid with response planning, we sought to explain this regional spread by assessing publicly available information.

The Study

The data analyzed were case counts, population data, and distances between affected and nonaffected districts (these distances are influential predictors in the spread of infectious diseases) (3–5). We first classified as affected those districts within Guinea (prefectures), Sierra Leone (districts), and Liberia (counties) that had reported to the World Health Organization ≥ 1 suspected, probable, or confirmed case of Ebola virus infection from the weeks ending March 29, 2014 (epidemiological week 13), through August 16, 2014 (epidemiological week 33) (2). For each district, we considered the week of its first reported case as the week it became affected (online Technical Appendix Figure 1, <http://wwwnc.cdc.gov/EID/article/21/3/14-1845-Techapp1.pdf>). We also identified the population-weighted geographic centroid (center of an area, adjusted for its population density) in each district and computed the distance from these centers to similar centers in each affected district.

We then created 4 regression models to calculate the weekly risk of a district being affected as a function of combinations of its population, the sum of inverse distances (SID) from all affected districts, and SID weighted by the number of new cases in affected districts over the preceding

3 weeks (online Technical Appendix Table 2). We chose the best model by examining how well it fit the data available through week 33 (August 16). We then evaluated how well the chosen model predicted that districts would become affected as the outbreak continued by comparing calculated probabilities that a district would become affected (at weeks 33, 36, and 39) to actual reports of newly affected districts over the subsequent 3-week periods (weeks 34–36 [period 1], weeks 37–39 [period 2], and weeks 40–42 [period 3], respectively). By using data available through week 42, we calculated probabilities that districts in countries bordering the 3 primarily affected countries (departments in Côte D'Ivoire, circles in Mali, departments in Senegal, sectors in Guinea-Bissau, and divisions in Gambia) would become affected.

We assumed that country and district borders were porous and that infected persons could not be prevented from moving into nonaffected areas (6–8). Reports from the field support this assumption, even after country borders were officially closed (9). We also assumed no heterogeneities in the capabilities of the different areas to identify and report cases and that aggregating case count reports into a weekly unit of analysis would blunt the effects of reporting delays. Our last assumption, for identifying an affected district, was that suspected and probable cases were as sensitive and specific as confirmed cases.

Among the 3 primarily affected countries, 39 districts were affected in 12 weeks (during weeks 13–33). The model that best explained this pattern was one in which the risk of a district becoming affected depended on its population and the SID from all affected districts to a nonaffected district and in which each inverse distance is multiplied by the sum of new cases within the past 3 weeks (weighted SID) (online Technical Appendix Table 2 and Figure 2). The overall average weighted SID was greater for districts during the weeks in which they became affected than for districts that had not yet reported cases by the same week (online Technical Appendix Figure 3, panel A).

Figure 1 shows the probabilities for specific districts becoming affected at weeks 33, 36, and 39. The ranking of districts by their probabilities on week 33 (Figure 1, panel A) illustrates the good fit of the model because 27 (87%) of the 31 districts ranked in the top half (most likely to become affected) were actually affected.

During weeks 34–36 (period 1), 4 districts became affected; during weeks 37–39 (period 2), 4 districts became affected; and during weeks 40–42 (period 3), 5 districts became affected. The model predicted well which districts would become affected during periods 1 and 3 (Figure 1,

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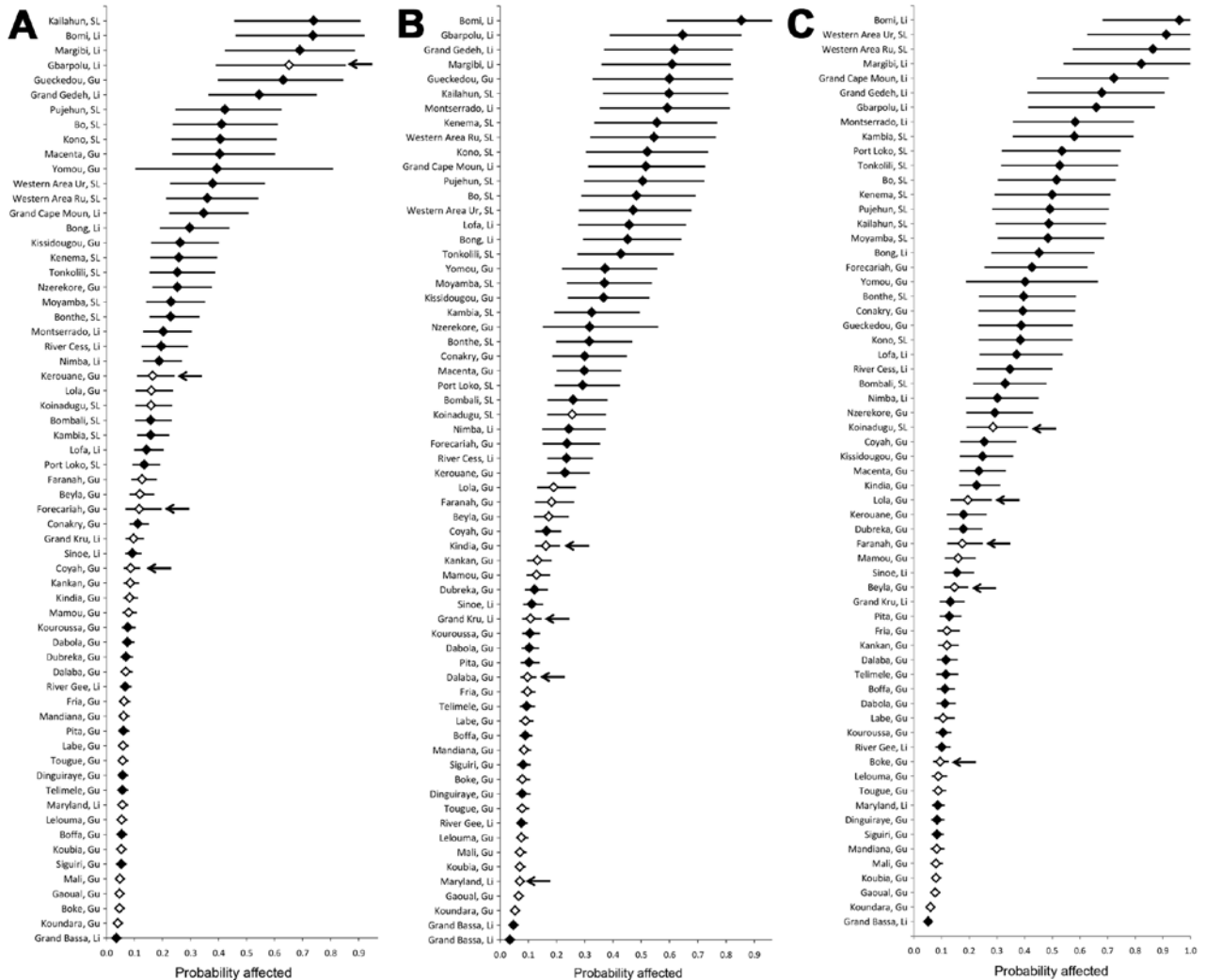


Figure 1. Probability predictions (with 95% CIs) for districts in countries primarily affected by Ebola virus infection in 2014, by week of analysis. A) Data available through week 33 (August 16). B) Data available through week 36 (September 6). C) Data available through week 39 (September 27). Diamonds indicate the probability that the districts should be affected at the time of the analysis. Filled diamonds indicate districts that were affected (i.e., had reported at least 1 case) at the date of the analysis. Black arrows identify those districts that became affected within 3 weeks of the date of analysis. SL, Sierra Leone; Gu, Guinea; Li, Liberia.

panels A, C); districts that became affected were predominantly among those with the highest calculated probabilities of becoming affected. The model did not predict as well which districts would become affected during period 2 (Figure 1, panel B).

Of 167 districts in the countries bordering the primarily affected countries, the predicted probability of becoming affected was >20% for 9 districts (calculated at week 42). The 3 top-ranked districts had the largest populations in their respective countries: Abidjan (Côte D’Ivoire), Bamako (Mali), and Pikine (Senegal); Bamako and Pikine reported cases in weeks 43 and 35, respectively. Also, among the top 10 districts, 5 were on or near the Côte D’Ivoire–Liberia border (Figure 2).

Conclusions

We identified spatial influences on the regional spread of Ebola virus infections. The risk of becoming affected by Ebola was significantly higher for nonaffected districts that had a larger population and that were closer to affected districts with higher case counts (online Technical Appendix Table 2 and Figure 2). Thus, it seems that data on population size and straight-line distances can serve as pragmatic alternatives to data on travel patterns between Guinea, Liberia, and Sierra Leone during the first 8 months of the outbreak. The correlation between the risk of becoming affected and distances and population size was sufficiently accurate for predicting which districts would next become affected. Furthermore, a high calculated probability of becoming affected

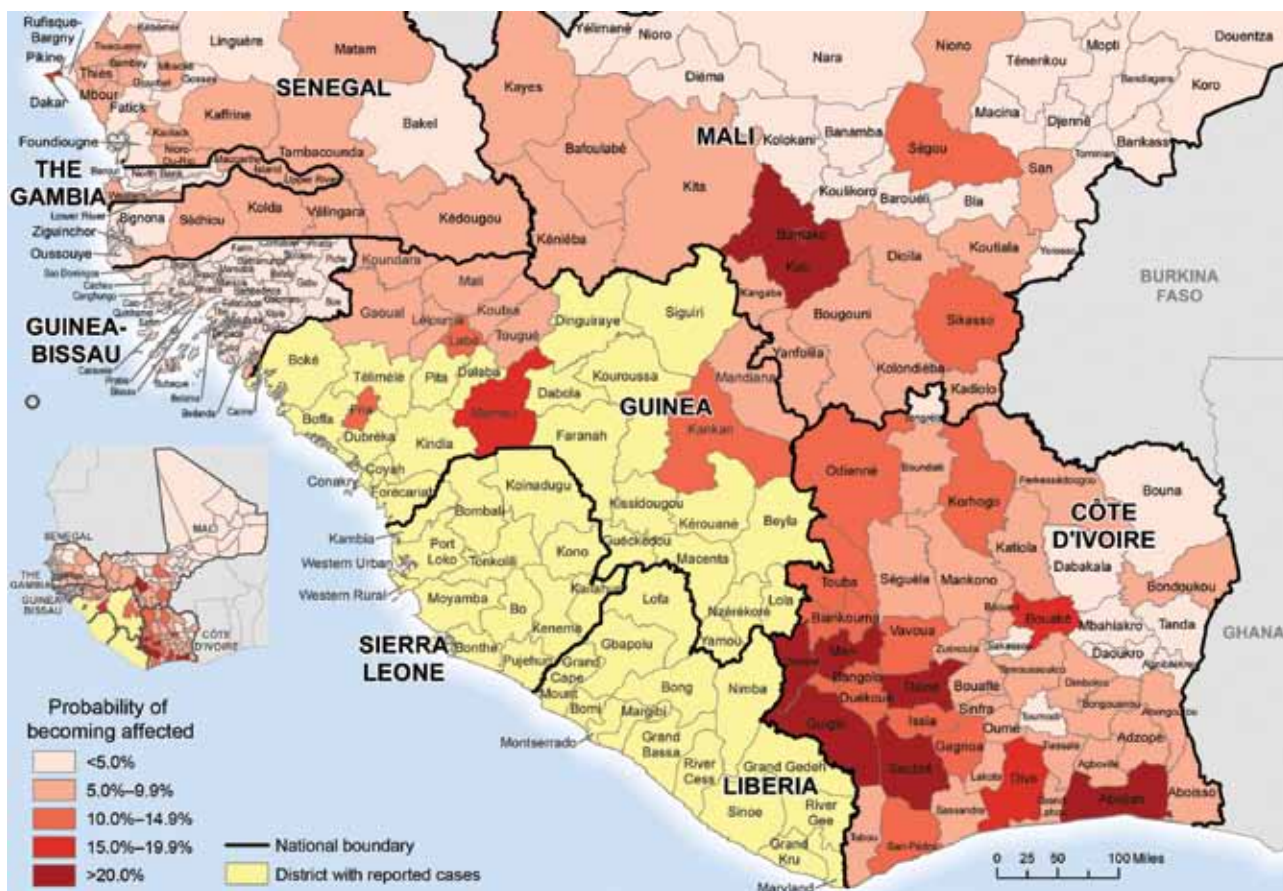


Figure 2. Predicted risk of districts becoming affected by Ebola virus infection (neighboring countries included) in 2014, based on data available through epidemiological week 42 (October 18, 2014).

for a district considered not affected might indicate the presence of undetected cases.

This analysis relied heavily on the accuracy of case reports and their timely documentation, but there are indications that extreme conditions in the affected countries resulted in incomplete records and reporting delays (10). These factors potentially contributed to errors in the identification of which week a district became affected. Consequently, we examined the potential effects of reporting delays (online Technical Appendix Table 2). Also, our results might have been influenced by our choice of administrative unit level to use for defining districts. (In our analysis, countries with smaller district units have less risk of being affected than countries with larger district units, if population densities are generally comparable.)

The good fit of our model, absent predictors for the influence of interventions, suggests that interventions (including border closings) were minimally effective at stemming regional spread of Ebola virus infection during the period analyzed. As the spread of the epidemic changes because of interventions and changes in human behavior, there is need to update and reevaluate the model fit and the parameters used.

We chose to not pursue data on travel patterns, despite their potential utility for explaining the spread of Ebola virus infection. Travel patterns may evolve as the outbreak progresses, and obtaining accurate data during an ongoing outbreak is challenging. We, therefore, focused on producing the simplest model.

Overall, our simple model shows that available case reports, population data, and distance data can be used to identify areas at risk of being affected in an outbreak of Ebola virus infection. Additionally, if the current pattern of spread in this outbreak continues, or if the outbreak takes hold in new countries, this model can be used to advocate for allocation of surveillance and control resources to non-affected areas.

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Technical Appendix

This Technical Appendix provides further details on the methods used as well as additional results.

Data and Definitions

Case Count Data: We obtained the cumulative number of confirmed, probable and suspect case counts for each of the 63 districts in Liberia, Sierra Leone, and Guinea from WHO Situation Reports posted weekly on the WHO's website (1). We defined a district as having become affected if it had least one suspect, probable, or confirmed Ebola case in the WHO reports. We considered the week a district first reported a case as the week it became "affected". We also used the case counts data from the WHO Situation Reports in our calculations of the weighted sum of inverse distances (see Calculations section below). We first identified the number of "new cases" in a single given week by subtracting the cumulative case count for a district in a given week from the cumulative case count reported for the week prior. We then summed the new cases values for every three week period in our outbreak dataset to obtain the number of new cases over the prior three weeks.

For some districts, defining the week a district became affected and calculating new cases was complicated by reductions in the cumulative case count from week to week or gaps in reporting. Technical Appendix Table 1 describes how case counts data were used to define the week of first report (i.e. affected) and for case count weighting in these special circumstances.

Other studies (2–4) examining the role of distance as a predictor of disease spread used confirmed cases only to determine when a new area had become affected. We did not rely on confirmed cases alone due to heterogeneity in the reporting delay of confirmed cases reported by country (5). For example, in Guinea (using data through week 33), the reporting of confirmed cases across all affected districts occurred on just 4 different weeks while the reporting of cases based on all types (i.e. including suspect and probable cases too) was spread across 8 weeks. Reports from the field indicated that this was the result of laboratory confirmation testing occurring via batch processing.

Geospatial Data: We obtained "district" and international boundary data from the GADM database of Global Administrative Areas, version 2.0 (<http://www.gadm.org>) and from the United Nations Mission in Liberia and the United Nations World Food Program via the United Nations Office

for the Coordination of Humanitarian Affairs' Humanitarian Response website (<http://www.humanitarianresponse.info/applications/data>). Districts were defined for the primarily affected countries as the equivalent of Prefectures in Guinea, Districts in Sierra Leone, and Counties in Liberia. For bordering countries, districts were defined as the equivalent of Départements (Departments) in Cote D'Ivoire, Cercles (Circles) in Mali, Départements (Departments) in Senegal, Sectors in Guinea-Bissau, and Divisions in Gambia. Population data [LandScan (2012)], was obtained from Oak Ridge National Laboratory (<http://web.ornl.gov/sci/landscan/>). ArcGIS v.10.2 (ESRI, Redlands CA) was used to calculate the population-weighted centroids for each district (or equivalent) and computing the geodesic distances between each district to all others. The population-weighted centroid was the center of a given area, adjusted for the density of the population within that area.

Technical Appendix Figure 1 shows the combination of the Geospatial data and the Case Counts Data (aggregated over 3 week periods for a simpler illustration), using data available through Week 39 [September 27]. At the time of our initial analysis (week-ending August 16, 2014, [epidemiological week 33]), the World Health Organization had reported 2,218, confirmed, probable and suspected cases in West Africa, with 523 in 14 of 34 districts in Guinea, 849 cases in 13 of 14 districts in Sierra Leone, and 846 cases among 12 of 15 districts in Liberia.

Calculations

Inverse Distances:

Sum of Inverse Distances (SID), Nonweighted:

Let X_i ($i= 1$ to n) be the set of unaffected districts at time t .

Let Y_j ($j= 1$ to N) be the set of affected districts at time t .

$$SID (X_i)_t = \sum_{j=1}^N 1 / D_{(X_i \rightarrow Y_j)}$$

Where $D_{(X_i \rightarrow Y_j)}$ is the population centroid-based geodesic distance between X_i to Y_j .

Weighted SID (wSID) by the rolling sum on new cases counts in the past three weeks:

Let $X_{(1 \text{ to } i)}$ be the set of unaffected districts at time t .

Let $Y_{(1 \text{ to } j)}$ be the set of affected districts at time t .

Let C_j be the number of new cases in the past three weeks (i.e. weeks $t-3, t-2$ and $t-1$) in district Y_j where $C_j \geq 1$.

$$\text{wSID } (X_i)_t = \sum_{j=1}^N C_j / D_{(X_i \rightarrow Y_j)}$$

Where $D_{(X_i \rightarrow Y_j)}$ is the population centroid-based geodesic distance between X_i to Y_j . $C_j \geq 1$ was used to prevent multiplication by zero (i.e. versus using where $C_j > 0$) and is justified by the results of Model 1 (see Technical Appendix Table 2). Model 1, which is statistically significant and uses a Nonweighted SID shows that all affected districts still have some influence on the probability of nonaffected districts becoming affected regardless of the number of new cases they have reported in the preceding three weeks

Goodness of Fit and Correlation:

We measured goodness of fit of the models to the data available through week 33 by assessing how well the models agreed with the set of districts reporting being affected at the time of analysis. To do this, we computed the predicted probability p_i of an individual district i being affected at each outbreak week (see Individual District Probabilities section below). Then we calculated the log likelihood (LL) for the set of districts already affected:

$$LL = \sum_i I_i * \log(p_i) + (1 - I_i) * \log(1 - p_i)$$

Where $I_i = 1$ if the district was officially affected and $I_i = 0$ when nonaffected. The larger the LL the better the fit.

We also computed a Partial Correlation coefficient for each model. This was the marginal contribution of a single predictor to reducing the unexplained variation in affected/nonaffected outcome. The partial correlation indicates the explanatory value attributable to the predictor.

All analyses were completed using SAS for Windows version 9.3 (SAS Institute Inc., Cary, NC, USA).

Model Comparisons

Technical Appendix Table 2 shows the results of the various models which were evaluated for their ability to explain the regional spread of Ebola. All of the models were statistically significant at the .0001 level (Wald Chi-Square test) when testing the joint effect of the predictors included in the model. Model 3 fit the data the best (i.e. largest LL) and had the best explanatory value [Partial Correlation total > 60%].

The LL measure is criticized because it does not take into account the number of parameters used in the model, however, when the models were evaluated using the Akai Information Criteria (AIC), which explicitly does so, Model 3 was still the best fitting model: Model 1= 307.0; Model 2=292.6; Model 3=283.7.

Reporting Delay Analysis:

Several districts reported a relatively high number of cases in the week in which they first reported having cases. We considered reporting delays as a possible reason for the high count (under the assumption that a portion of these cases should have been reported in the prior week) and conducted an analysis to examine the impact on our results. In this analysis we adjusted the number of cases at the week of first report when it was greater than 10 [5 occurrences out of the 39 districts having reported cases by week 39] by distributing the case count over two weeks: one half remained in the same week and the other was assigned to the prior week. Technical Appendix Table 2 shows the results of this analysis. Models 1 and 4 saw slight improvement in their goodness of fit, but in the better fitting models [2 and 3], there was no improvement seen.

Internal Validation:

We randomly eliminated 10% (n=6) of districts from the outbreak data available through week 33 and fit Model 3 to this dataset. Afterwards, we examined whether the predicted individual probability of becoming affected for the eliminated districts (calculated using the original model with the full complement of data) fell within the 95% confidence interval generated by the model without these districts. We found that all probabilities fell within the 95% CI ranges, suggesting that the model based on the full dataset was appropriate.

Individual District Probabilities

In order to calculate the individual probabilities of a particular district becoming affected we used the maximum likelihood (ML) method to fit Model 3 to the outbreak data and obtain estimate values for the parameters α , β_1 and β_2 . The results of the initial ML estimation based on data available through week 33 are presented in Technical Appendix Table 3. Technical Appendix Figure 2 shows the resulting relationship between the predictors in Model 3 and the probability of becoming affected (also based on data through week 33).

As the outbreak continued, Model 3 was refit (i.e. new parameter values obtained for α and β) to the data at week 36, and again at weeks 39 and 42, in order to update the predicted probabilities for individual districts (Figures 1 and 2). The updated fit at week 42 was used to calculate the probabilities

for districts among the four countries bordering those primarily affected by the Ebola outbreak (Figure 2).

Additional Results

After determining the wSID parameter was significant in all main models we examined the differences between the wSID between affected and unaffected districts at each outbreak week. These results are shown in Technical Appendix Figure 3A. A discernable difference between the average wSID among affected and unaffected districts is apparent at weeks 29 through 33, but not in prior outbreak weeks. This may suggest that the relationship between distance and the probability of being affected only becomes influential at some threshold: At week 29 the difference in the overall wSID for districts that became affected that week and those that did not was 0.00035. Additionally, when we examined the differences between the average wSID in affected and unaffected districts within each country individually we did not observe a similar pattern for weeks 29 through 31 (Technical Appendix Figure 3B). This corroborates the lesser fit of Model 4 Reduced (Technical Appendix Table 2), which examined each country individually. It also suggests that border closings have not had a great deal of impact in slowing the cross-border spread of disease; in-line with our assumption that borders were porous.

Technical Appendix Table 1. Data definitions used for special data scenarios

Data scenario	Week definition	Case count weighting
Districts initially reporting suspect cases only and which then reported 0 cumulative cases in a later week due to invalidation of suspect cases through laboratory testing	We used the most recent week in the outbreak after which the cumulative case count remained above 0 as the week in which the district became affected.	Weekly counts comprised of suspect cases which were later invalidated were changed to 0 values
Districts with gaps in reporting	We assumed that there was no reversion back to unaffected during the weeks with absent data. We used the earliest week with reported cases as the week in which the district became affected.	During reporting gap weeks we used the number of cases reported in the week just prior to the reporting gap.
Affected districts with no new cases in a particular week	NA	Case count weighting = 1 (otherwise the inverse distance of that district would not contribute to the wSID)

Technical Appendix Table 2. Summary of models used to characterize the spread of Ebola to nonaffected districts - analysis completed on data available through week 33 (August 16, 2014)

Model	Probability of becoming affected	Log-likelihood (LL)		Partial Correlation*
		No adjustment	Reporting Adjusted†	
Model 0 (Intercept only)	$1/1 + e^{-\alpha}$	-165.03 (ns)	-165.03 (ns)	Not applicable
Model 1 (SID)	$1/1 + e^{-(\alpha + \beta_1 \text{SID})}$	-159.49	-151.62	29.2
Model 2 (wSID)	$1/1 + e^{-(\alpha + \beta_1(\text{wSID}))}$	-144.29	-144.33	36.0
Model 3 (wSID + Population)	$1/1 + e^{-(\alpha + \beta_1(\text{wSID}) + \beta_2(\text{Population}))}$	-138.85	-139.19	60.6
Model 4‡ (wSID _G + wSID _L + wSID _S)	$1/1 + e^{-(\alpha + \beta_1(\text{wSID}_G) + \beta_2(\text{wSID}_L) + \beta_3(\text{wSID}_S))}$	-151.06	-139.64	27.0
Model 4 Reduced‡ a) only Guinea data (wSID _G)	$1/1 + e^{-(\alpha + \beta_x(\text{wSID}_y))}$	a) -65.3 (ns)	Not evaluated	Not evaluated
b) only Sierra Leone data (wSID _S)	Where $\beta_x \text{wSID}_y = \beta_1(\text{wSID}_G), \beta_2(\text{wSID}_L), \text{ or } \beta_3(\text{wSID}_S)$	b) -41.5		
c) only Liberia data (wSID _L)	From Model 4's equation above	c) -47.6 (ns)		

*ns, the difference between the model with covariates and the model with the intercept only was not statistically significant at the .0001 level.

† Partial correlations were calculated for the model with "No adjustment" for case reporting delays. For models with more than one parameter [Models 3 and 4] the value shown is the sum of the partial correlation coefficients as follows. Model 3; wSID=37.9 and Population=22.7. Model 4; wSID_G=0.1, wSID_L=-0.1, wSID_S=27.0.

‡ When the number of cases at the week of first report was greater than 10 we halved the number of cases at first report and made the week of first report 1 week earlier, by assigning half the cases to that week.

‡ Subscripts G, S, and L correspond to Guinea, Sierra Leone, and Liberia, respectively.

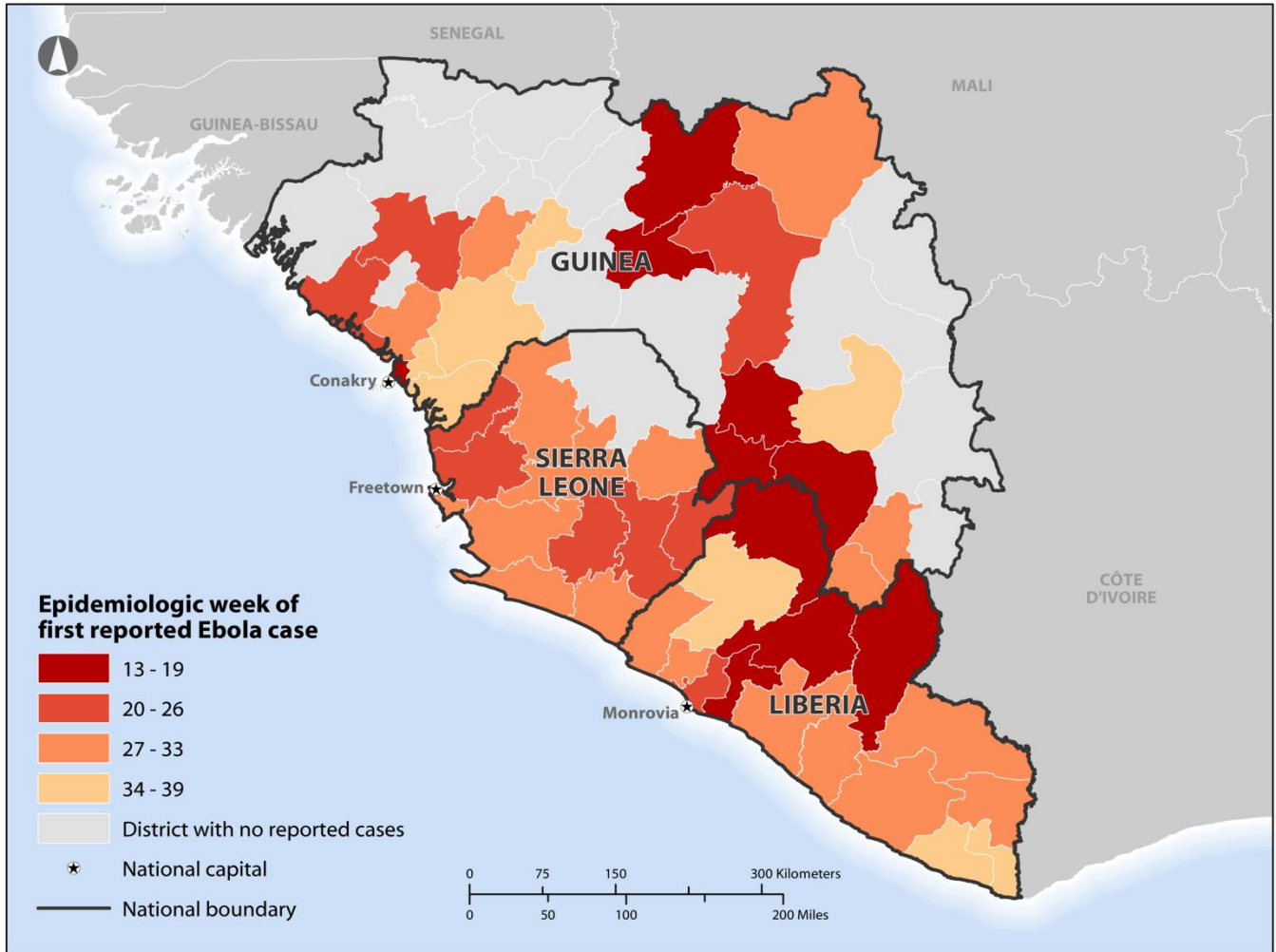
Technical Appendix Table 3. Results of maximum likelihood estimation for Model 3; completed on data available through week 33 (August 16, 2014)

Parameter	Symbol	Estimate	Standard Error	Wald Chi-Square	Significance Level	Partial Correlation
Intercept	α	-5.1556	0.3950	170.3755	<.0001	
wSID	β_1	1794.8	255.4	49.3937	<.0001	0.3789
Population	β_2	2.628E-6	6.041E-7	18.9282	<.0001	0.2265

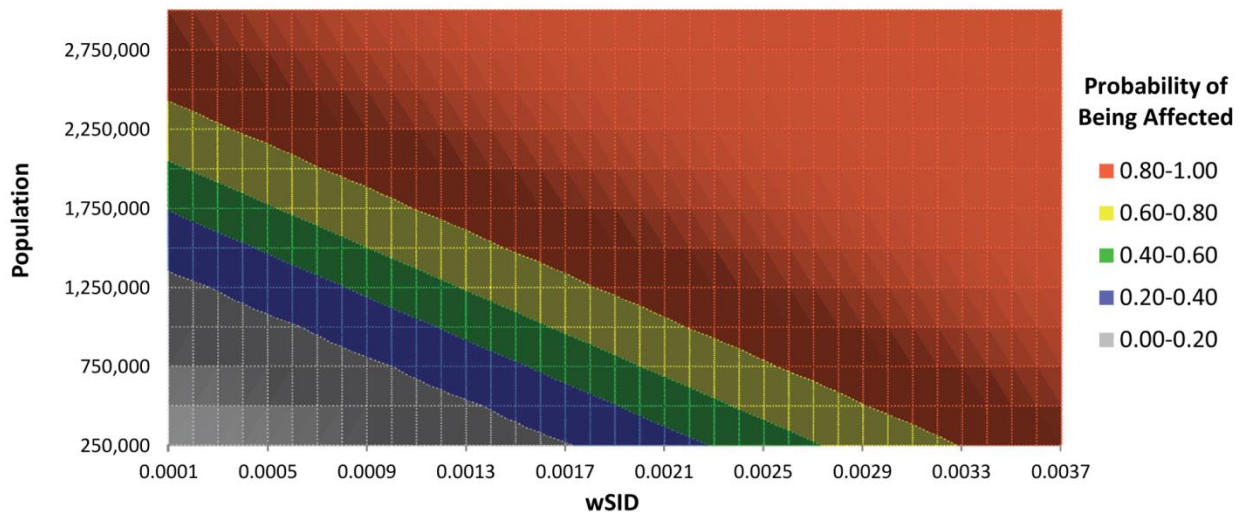
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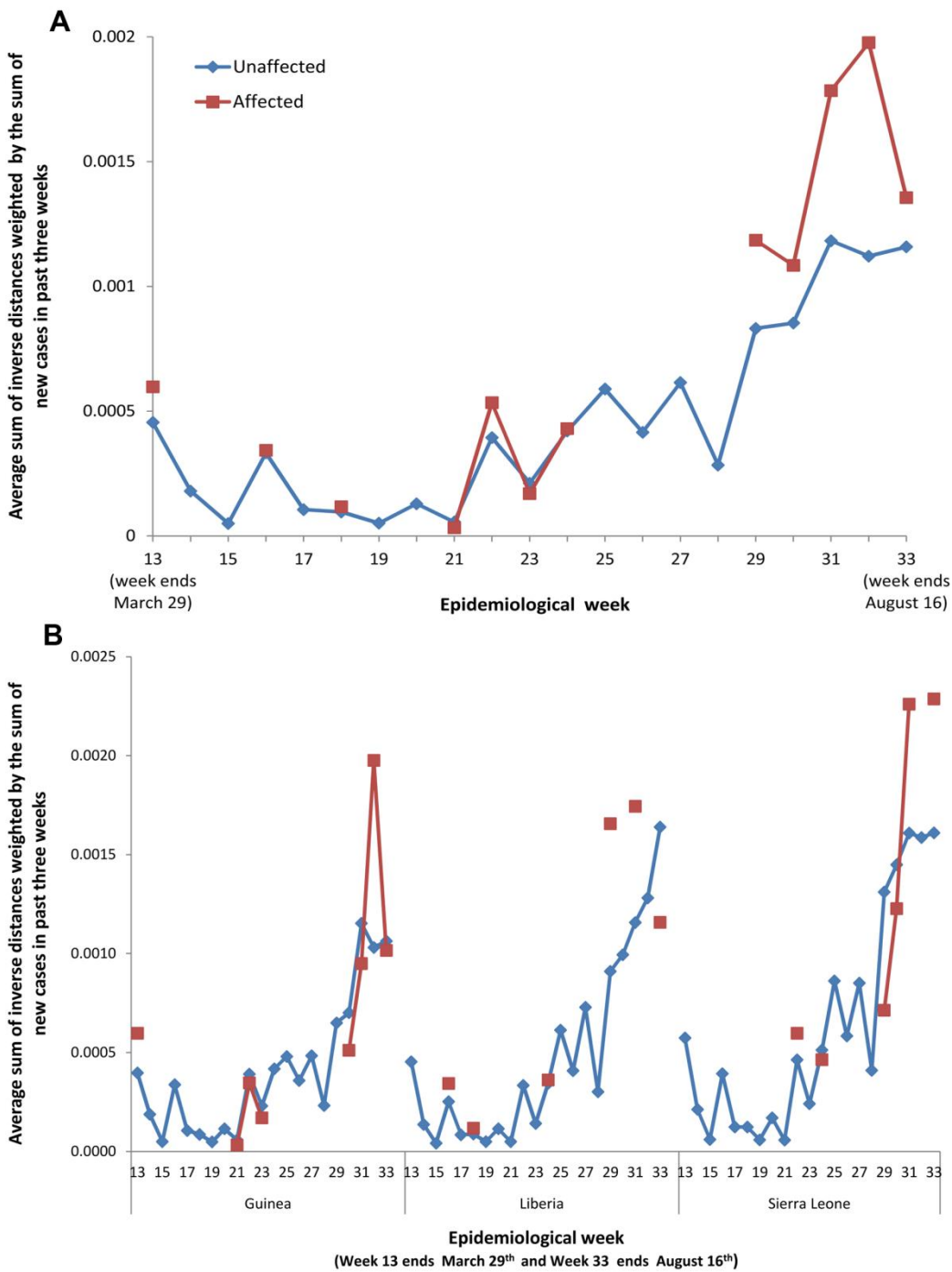
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Technical Appendix Figure 1. Map of the primary Ebola affected countries by week districts became affected (using data available through week 39 [September 27] (2) Notes: International borders were closed as follows: Sierra Leone, June 11th [week 24]; Guinea, August 9th [week 32]; Liberia, August 22 [week 34] (6–8).



Technical Appendix Figure 2. Predicted probability of a district becoming affected as a function of its population and the weighted-SID to affected areas (fitted to data available through week 33 [August 16])



Technical Appendix Figure 3. Average weighted-SID by outbreak week and affected status for all primarily-affected countries (Panel A) and for each individual country (Panel B) Notes: The average of the weighted-SID's influence (wSID) on districts that were affected (red-square marker) is compared here to the average (wSID) for nonaffected districts (blue diamond marker) at each outbreak week. Districts became affected on just 12 of the outbreak weeks, resulting in the gaps in the affected line (as of week 33, when this analysis was completed). A discernable difference between the average wSID among affected and nonaffected districts is apparent when all countries are shown together at weeks 29 through 33 (Panel A).