Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: WHO Ebola Response Team. West African Ebola epidemic after one year — slowing but not yet under control. N Engl J Med 2015;372:584-7. DOI: 10.1056/NEJMc1414992

Supplementary Appendix

West African Ebola Epidemic After One Year: Slowing But Not Yet Under Control

WHO Ebola Response Team

Junerlyn Agua-Agum, M.Ph., Archchun Ariyarajah, M.Sc., Bruce Aylward, M.D. Isobel M. Blake, Ph.D., Richard Brennan, M.D., Anne Cori, Ph.D., Christl A Donnelly, Sc.D., Ilaria Dorigatti, Ph.D., Christopher Dye, D.Phil., Tim Eckmanns, M.D., Neil M Ferguson, D.Phil., Pierre Formenty, M.D., Christophe Fraser, Ph.D., Erika Garcia, M.Ph., Tini Garske, Ph.D., Wes Hinsley, Ph.D., David Holmes, B.Sc., Stéphane Hugonnet, M.D., Swathi Iyengar M.Sc., Thibaut Jombart, Ph.D., Ravi Krishnan, M.Sc., Sascha Meijers, B.Sc., Harriet L. Mills, Ph.D., Yasmine Mohamed, B.Sc., Gemma Nedjati-Gilani, Ph.D., Emily Newton, B.Sc., Pierre Nouvellet, Ph.D., Louise Pelletier, M.D., Devin Perkins, B.A., Steven Riley, D.Phil., Maria Sagrado, M.Sc., Johannes Schnitzler, M.D., Dirk Schumacher, M.Sc., Anita Shah, M.Ph., Maria D Van Kerkhove, Ph.D., Olivia Varsaneux, M.Sc., Niluka Wijekoon Kannangarage, M.B.B.S.

World Health Organization (WHO), Geneva (J.A.-A., A.A., B.A., R.B., C.D., T.E., P.F., E.G., D.H., S.H., S.I., R.K., S.M., E.N., D.P., L.P., I.S., M.S., D.S., A.S., O.V., N.W.K.). Robert Koch Institute, Department for Infectious Disease Epidemiology, Berlin, Germany (T.E., D.S.) The Medical Research Council Centre for Outbreak Analysis and Modelling, WHO Collaborating Centre for Infectious Disease Modelling, Department of Infectious Disease Epidemiology, Imperial College London, United Kingdom (I.M.B., A.C., C.A.D., I.D., N.M.F., C.F., T.G., W.H., T.J., H.L.M., G.N.-G., P.N., S.R., M.D.V.K.)

Correspondence: Christl A Donnelly (c.donnelly@imperial.ac.uk), Neil M Ferguson (neil.ferguson@imperial.ac.uk), Christopher Dye (dyec@who.int)

Contents

Data Sources

Details of the ebola virus disease (EVD) data collection have been described previously[1]. Briefly, data on confirmed, probable or suspected EVD cases were collected using standardized viral hemorrhagic fever (VHF) data collection forms. Cases were identified through clinical care at treatment facilities or via contact tracing in Guinea, Liberia, Nigeria and Sierra Leone. We focus our analyses on the three most heavily affected countries: Guinea, Liberia and Sierra Leone, unless otherwise stated.

Analyses reported here of age distribution, incubation periods, serial intervals, other delay distributions, case fatality rate (CFR), demography and signs and symptoms of disease used the VHF patient databases from 24, 25 and 24 November from Guinea, Liberia and Sierra Leone, respectively.

However, delays in entering full case details into the VHF patient databases meant that to provide timely case projections and estimates of the epidemic growth rate, it was necessary to supplement the VHF line-list data with case data reported by the affected countries in their daily situation reports. The daily situation reports provide timely reports of recently detected cases, but are subject to retrospective revision, meaning the VHF patient databases provide the most definitive (but delayed) picture.

By comparing the VHF patient databases and situation report case numbers, we determined the latest date on which the patient databases provided an accurate depiction of case trends (by date of onset) for each district in Guinea, Liberia and Sierra Leone. This date varied between late September and late November 2014 depending on district, reflecting wide geographic variation in how quickly cases are entered into the patient database. After the last reliable date for each district we substituted the case numbers reported in the daily situation reports, allowing for a 4-day delay from symptom onset to case report (so, for example, the estimated number of EVD cases in Montserrado with symptom onset on 20 November was taken to be the number of cases reported in the daily situation report on 24 November).

Supplemented daily incidence time series were derived for confirmed and probable cases and for confirmed, probable and suspected cases for the presentation of trends in incidence, estimation of the epidemic growth rate (R_t) and projections of case numbers.

Case definitions were provided by WHO[2].

Data Cleaning

Cleaning of the data has been described in the supplementary appendix of our original paper[1]. As a refinement of the procedures described there, we improved the algorithm for identifying errors in reported dates and for inferring onset and notification dates for cases where these were missing. We also removed duplicate records from the data for the current analysis (i.e. records potentially describing the same person).

Date cleaning

Delays between 14 key events in disease progression were evaluated for each patient, including onset date, current and past hospitalization and hospital discharge dates, isolation dates, sample collection and test dates, dates of death and funeral and notification and outcome completion dates.

Delays outside intervals specified for each pair of delays (insert table) were flagged as unrealistic. For each person, the dates giving rise to the most unrealistic delays were set to NA and the delays re-evaluated until no unrealistic delays remained.

Inferring onset and notification dates

For inferring onset and notification dates we changed the order of preference in which we used the available dates compared to the algorithm described previously:

We inferred dates of onset and notification for patients where these were missing based on information learned from cases with complete date records. For example, for a person with missing onset date but recorded hospitalization date, we inferred the onset date to have been x days prior to the notification date, where x was the country-specific median observed delay between onset and hospitalization dates for patients where both dates were recorded. For countries with less than 10 patients who had both required dates recorded, the overall median across all countries was used instead. We considered the date of hospitalization to be most reliable, followed by date of death, date of discharge, date of isolation, date of symptom onset, date of notification and date of outcome completion, in that order. Hence for inferring dates of symptom onset, we used the following set of rules:

- If the date of hospitalization was available then we inferred the date of symptom onset as the date of hospitalization minus the median onset-to-hospitalization delay.
- Otherwise, if the date of death was available then we inferred the date of symptom onset as the date of death minus the median onset-to-death delay.
- Otherwise, if the date of hospital discharge was available then we inferred the date of symptom onset as the date of hospital discharge minus the median onset-to-hospital discharge delay.
- Otherwise, if the date of isolation was available then we inferred the date of symptom onset as the date of isolation minus the median onset-to-isolation delay.
- Otherwise, if the date of notification was available then we inferred the date of symptom onset as the date of notification minus the median onset-to-notification delay.
- Otherwise and finally, if the date of outcome completion was available then we inferred the date of symptom onset as the date of outcome completion minus the median onset-to outcome-completion delay (unless sample size <10 and then the overall median is used).

For inferring dates of notification, we similarly used dates of hospitalization, death, hospital discharge, isolation, symptom onset, and outcome completion dates, in that order of preference.

Rules for identifying duplicate records

All names were encrypted using a one-way hashing algorithm prior to data analysis.

We created a list of potential duplicate records by finding pairs or groups of individuals in each country database which match on surname (anonymised), other names (anonymised), country of residence and gender. When we compared entries which were missing, we always regarded them as a possible match, i.e. missing will match another missing, and missing will match a reported name, etc. (except for surname which we required to not be missing).

We then imposed the constraint that these pairs or groups of individuals must also match on at least two of the following:

1. Date of onset or date of report or date of death
2. District of residence
3. Age (in years)
4. Phone number (anonymised)
5. Named contact (anonymised)

We further constrained age such that the difference in reported ages between all pairs of individuals in a matched group must be less than 10 years.

Lastly, we constrained dates such that: if neither date of onset nor date of report matched exactly, the difference in dates of onset between individuals in a group needed to be ≤7 days. If date of onset was missing, the difference in dates of report between individuals needed to be ≤7 days. If date of report was missing as well, date of death must match exactly.

Rules for merging duplicate records

For a pair of records identified as duplicates according to the rules above, we merged the records into a single one according to the following rules.

- For all fields which were identical, we kept that entry.
- For all fields where one entry was missing and not the other, we kept the non-missing entry.
- If fields were different, we defined the most recent entry, based on these dates by order of preference (i.e. we took the first non-missing date): First Save Time (the timestamp of record creation); Date of Report; Date of Onset; Date of current hospital admission. We used this to merge other fields as follows:
- **Epidemiological case definition (EpiCaseDef):**
    - If possible: we took the most recent entry.
    - If not possible (dates missing or dates are the same): we took the epidemiological case definition (EpiCaseDef) in order of preference: Confirmed, Not a case, Probable, Suspected, Excluded.
- **Dates fields:**
    - If EpiCaseDef was different in the duplicate records: we took date in order of preference from EpiCaseDef Confirmed, Probable, Suspected, Not a case, Excluded.
    - If EpiCaseDef was the same: we checked whether dates were within ≤7 days of each other,
        - If so, we took most recent date.
        - Otherwise, we issued a warning and put missing.
- **Age:**
    - We took the median (rounded up to nearest year).
- **Village fields and Parish fields and District fields:**
    - We concatenated the entries, separated by a "+".
- **Hospitals (including current hospital and hospital at death or discharge):**
    - If possible: we took the most recent entry.
    - Otherwise, we concatenated the entries, separated by a "+".

- **Final Status:**
  - If at least one date of report was missing, we kept "dead".
  - If the date of report for the "dead" was on or after the date of report for the "alive", we kept "dead".
  - Otherwise, we issued a warning and put missing.
- **Health Care Worker (HCW):**
  - No vs. Yes was merged as Yes (i.e. if ever a HCW, we recorded the status as HCW).
- **HCW Position and HCW Facility**
  - We concatenated the entries, separated by a "+".
- **Occupation other than HCW:**
  - If possible: we took the most recent entry.
  - Otherwise, we concatenated the entries, separated by a "+".
- **Symptoms indicators:**
  - No vs. Yes was merged as Yes (i.e. if ever had that symptom, we recorded the symptom as Yes).
- **Symptoms – temperature:**
  - We took the median.
- **Symptoms comments:**
  - We concatenated the entries, separated by a "+".
- **All Named Contacts (x3 for non-funeral exposures and x2 for funeral exposures):**
  - We concatenated all contacts named by either individual in a pair to the new merged record (extending the number of Contact or Funeral entries, if needed), only recording doubly named contacts once (in which case, we take the first entry). All information on contacts including dates, relationship to contact, etc. were merged using this rule.
- **All other fields:**
  - We set to missing.

Results of merging duplicate records

Before merging duplicate records the VHF databases contained information on 25,068 individuals (of which 17,759 were recorded as confirmed, probable or suspected EVD cases); after merging there were data on 24,124 individuals (of which 16,964 were recorded as confirmed, probable or suspected EVD cases). In total, 3.7% of individuals (4.5% confirmed, probable or suspected EVD cases) were removed.

There were differences by country: Sierra Leone had the largest proportion, with 5.2% of all individuals (6.5% of confirmed, probable or suspected EVD cases) removed, Liberia had 2.9% of all individuals (3.2% of confirmed, probable or suspected EVD cases) removed and Guinea 0.90% of all individuals (0.96% of confirmed, probable or suspected EVD cases) removed.

Presentation of results by Case Definitions

All methods used have been previously described[1]. For each result, we present the results for confirmed and probable EVD cases reported by Guinea, Liberia and Sierra Leone, and separately for confirmed, probable and suspected EVD cases reported by Guinea, Liberia and Sierra Leone.

EVD Incidence

By Country

For each country, EVD incidence by case definition[2] is shown in Figure S1. In Guinea, few suspected EVD cases are reported, whereas the ratios of confirmed to probable and probable to suspected cases have varied in Liberia and Sierra Leone over time. The EVD data presented in Figure S1 are based on the supplemented daily incidence time series as described in the Data Sources section of this document.

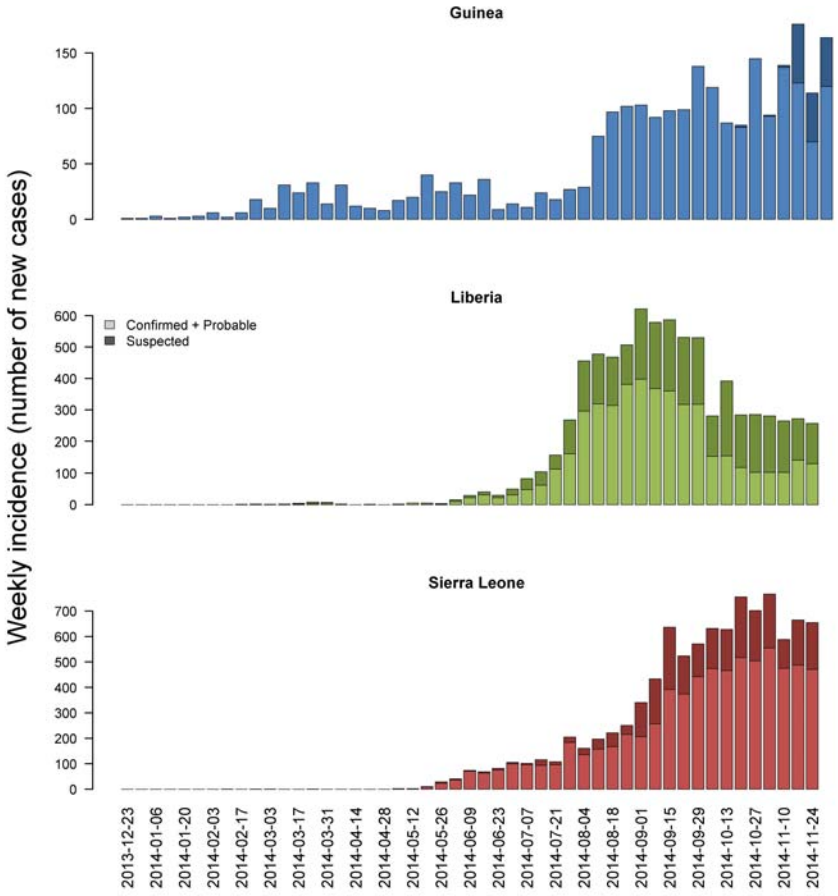

Figure S1. Weekly Incidence of confirmed, probable and suspected EVD cases for Guinea (blue, to week starting 1 December 2014), Liberia (green, to week starting 24 November 2014) and Sierra Leone (red, to week starting 24 November 2014) plotted by week of symptom onset (denoted by the first day of the week and based on the supplemented daily incidence time series as described in Data Sources). Shading indicates confirmed and probable (lighter shading) and suspected (darker shading) EVD cases.

By District

National incidence patterns arise from very different dynamics at the district level for both confirmed and probable EVD cases (Figures S3-6) and confirmed, probable and suspected EVD cases (Figures S7-10). The locations of districts are presented in Figure S2. The five districts within Conakry (Dixinn, Ratoma, Kaloum, Matam and Matoto) are presented collectively as Conakry. Freetown and

Western Rural are presented collectively as Western Area. These two aggregations were made because the districts within these areas were not specified for some of the EVD cases.

Gueckedou, the first affected district in Guinea, maintained consistent incidence for many weeks until early September, when incidence started to decline. In Liberia, the most heavily affected districts of Montserrado (which includes the capital city Monrovia) and Margibi have seen a substantial decrease in cases in recent weeks, but transmission has persisted into December. In Sierra Leone, the districts of Port Loko and Western Area have been the cause for most concern in the last 3 months, though previous increases in incidence appear to now have slowed, and may have reversed. However, given the inevitable delays in reporting (see ref 1 and Tables S5-S8), it will be mid-January before it is possible to conclude definitively whether the incidence of new cases in those districts has been brought under control.

Figure S2. Map of districts for Guinea, Liberia and Sierra Leone

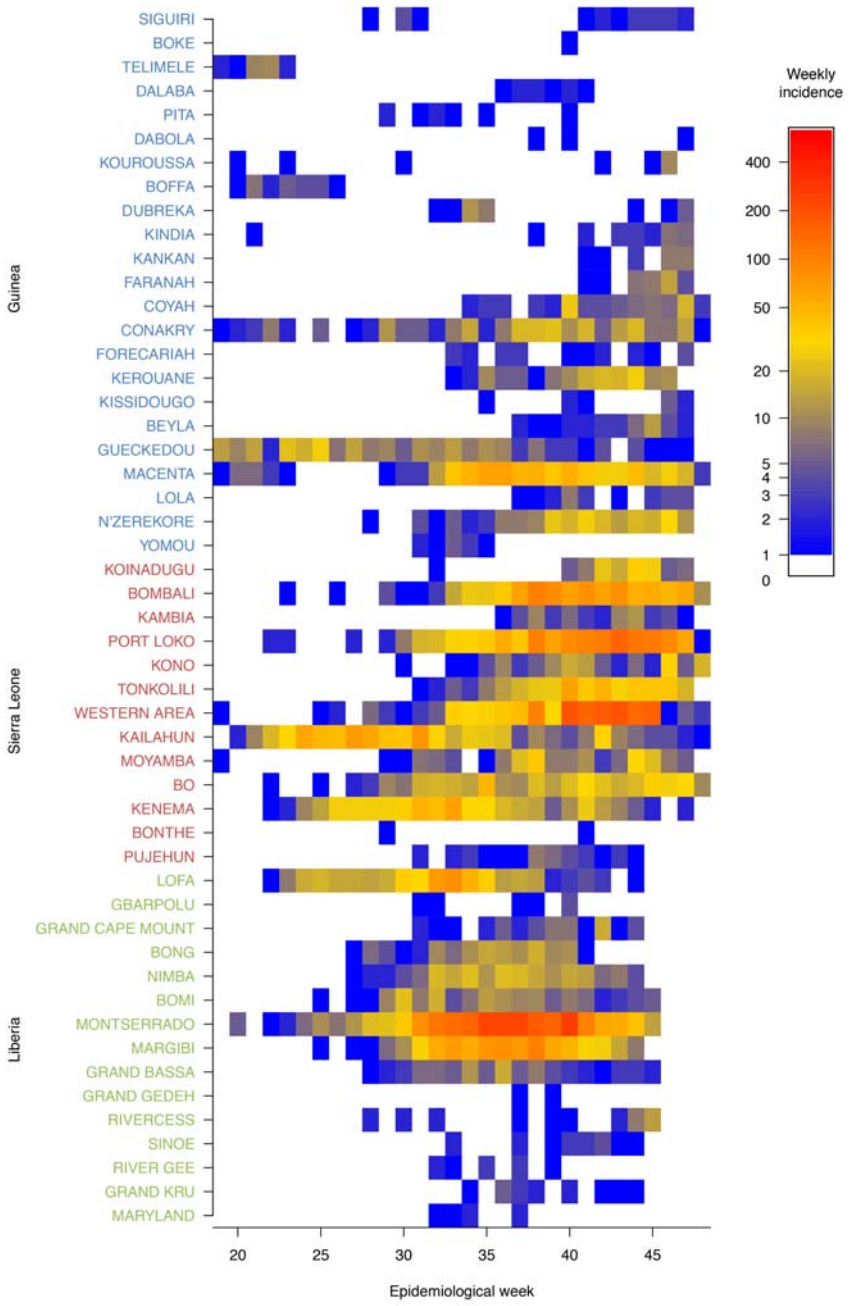

Figure S3(A): Weekly incidence of confirmed and probable EVD cases by week of symptom onset (based on VHF databases). Data are for all districts in Liberia (labels in green, to week starting 24 November 2014), Sierra Leone (labels in red, to week starting 24 November 2014) and Guinea (labels in blue, to week starting 24 November 2014) from which at least one case has been reported. Shading indicates the number of new cases with onset that week, as per the legend. On the y-axis, districts within country groups are ordered by increasing latitude of the district centroid from bottom to top. The first day of week 1 for the x-axis is Monday 30 December 2013. Week 20 started on Monday 12 May 2014 and week 40 started on Monday 29 September 2014.

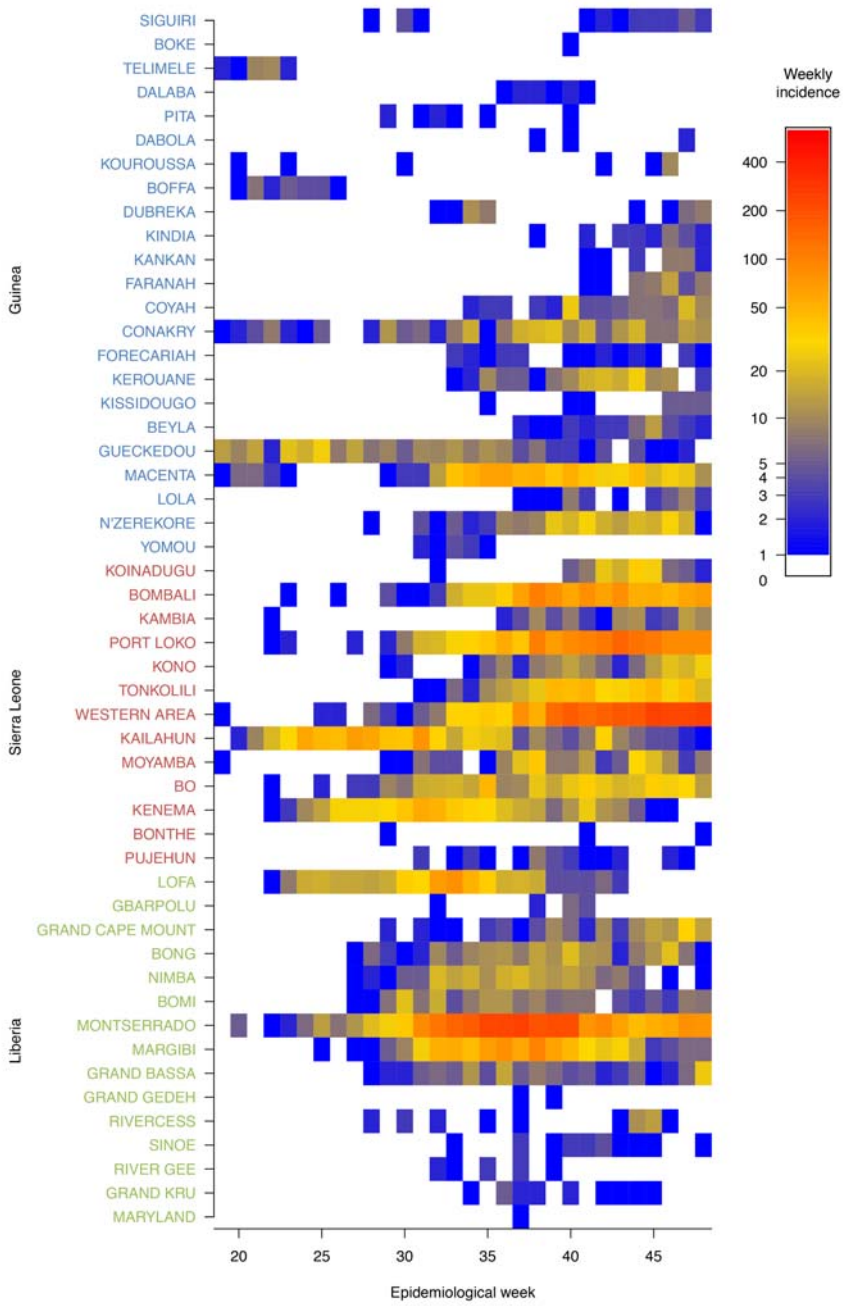

Figure S3(B): Weekly incidence of confirmed and probable EVD cases by week of symptom onset (based on the supplemented daily incidence time series as described in Data Sources). Data are for all districts in Liberia (labels in green, to week starting 24 November 2014), Sierra Leone (labels in red, to week starting 24 November 2014) and Guinea (labels in blue, to week starting 24 November 2014) from which at least one case has been reported. Shading indicates the number of new cases with onset that week, as per the legend. On the y-axis, districts within country groups are ordered by increasing latitude of the district centroid from bottom to top. The first day of week 1 for the x-axis is Monday 30 December 2013. Week 20 started on Monday 12 May 2014 and week 40 started on Monday 29 September 2014.

Guinea

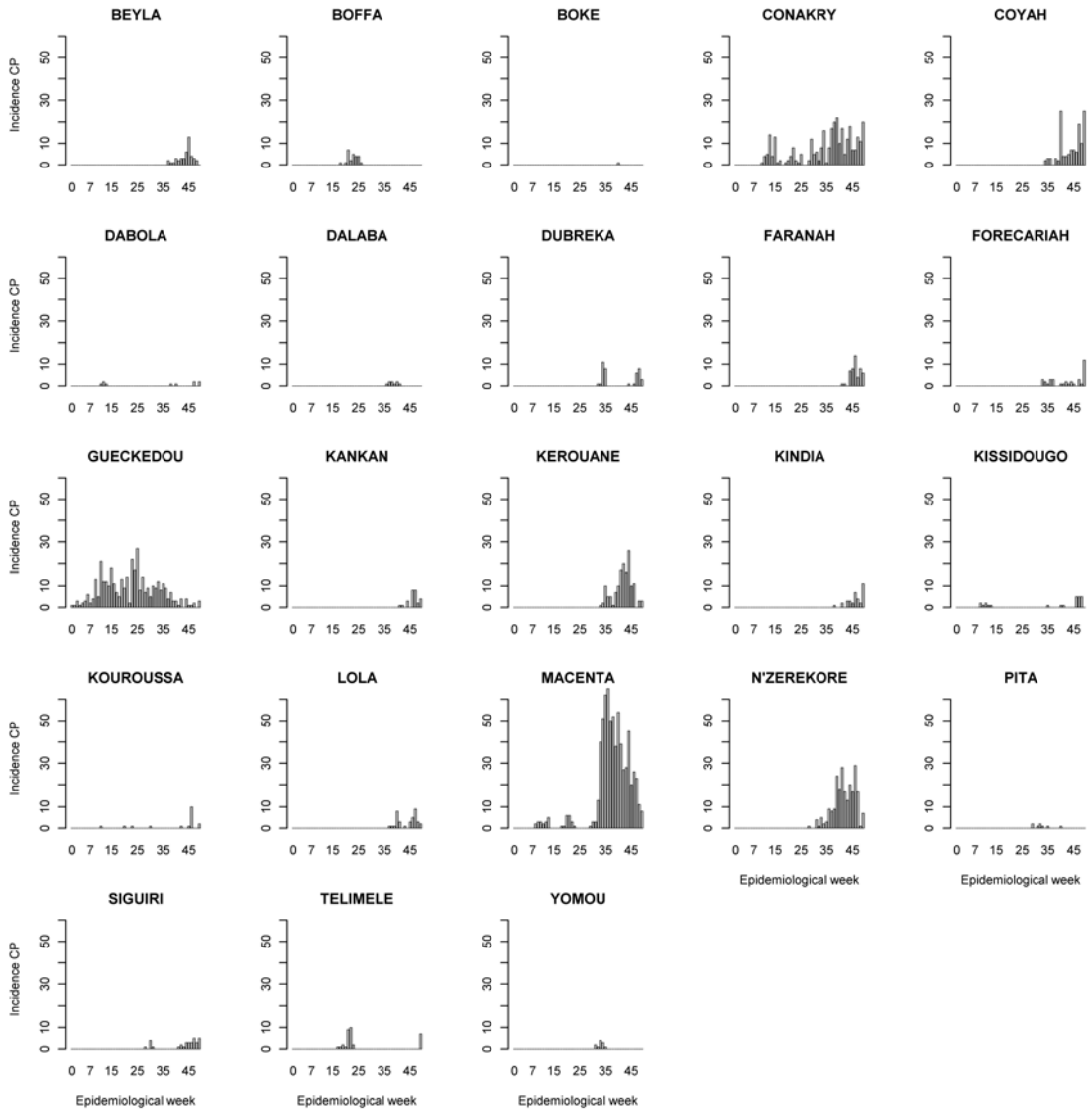

Figure S4: Weekly incidence of confirmed and probable EVD cases in Guinea by district plotted by week of symptom onset (based on the supplemented daily incidence time series as described in Data Sources, to week starting 1 December 2014). The first day of week 1 for the x-axis is Monday 30 December 2013. Week 20 started on Monday 12 May 2014 and week 40 started on Monday 29 September 2014.

Liberia

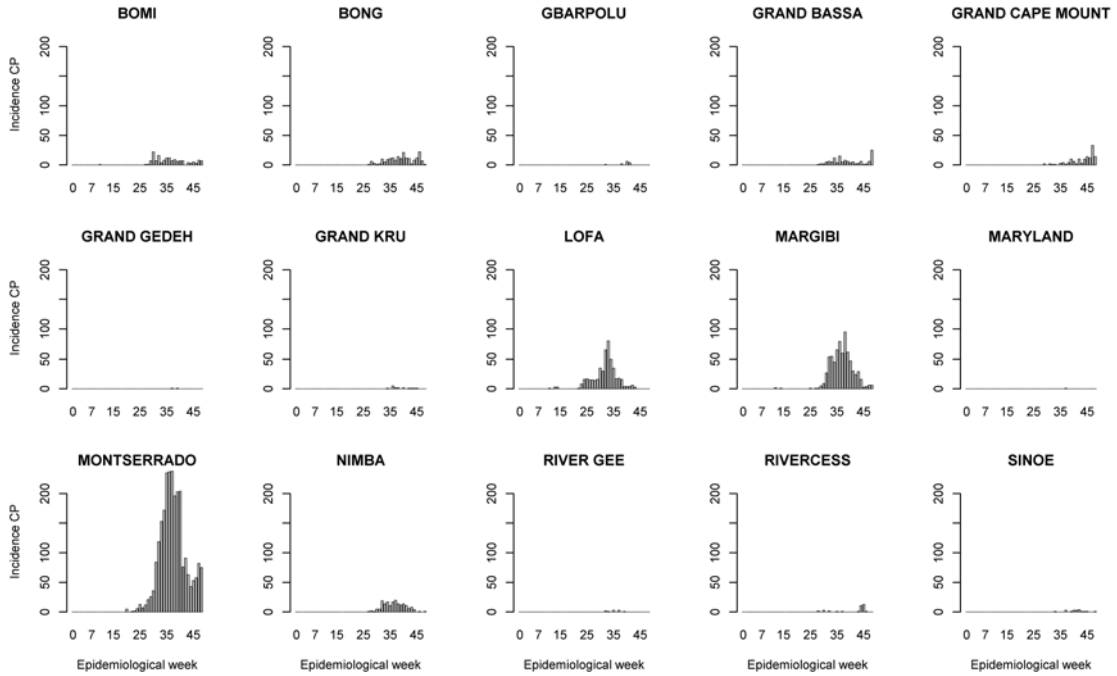

Figure S5: As Figure S4 but for districts in Liberia (to week starting 24 November 2014).

Sierra Leone

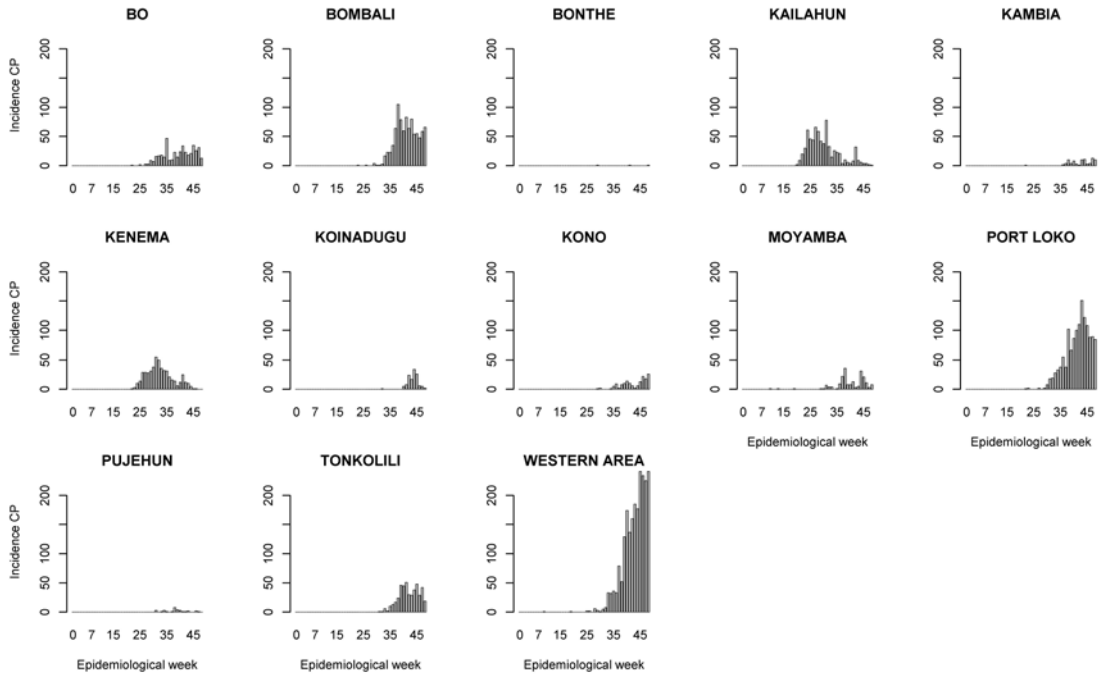

Figure S6: As Figure S4 but for districts in Sierra Leone (to week starting 24 November 2014).

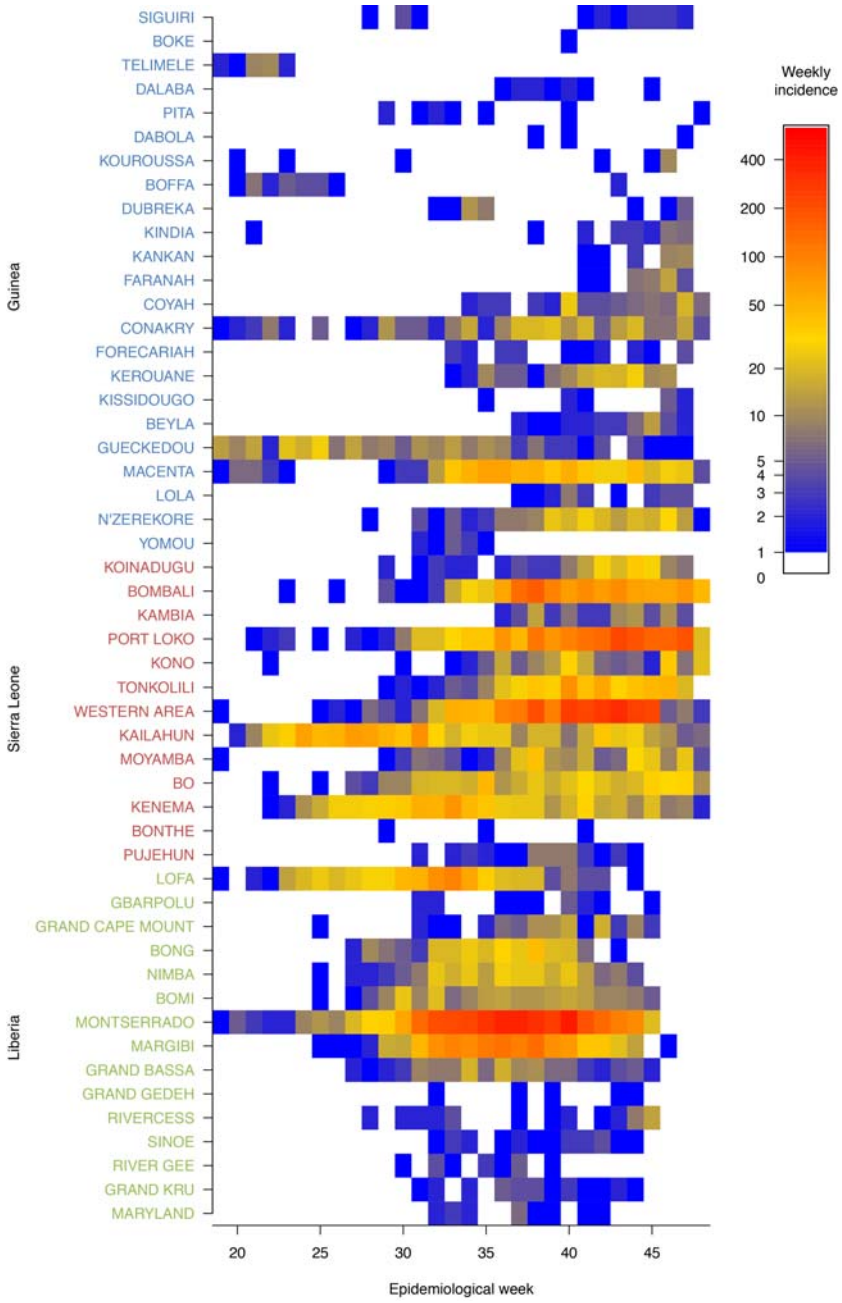

Figure S7(A): As Figure S3(A) for confirmed, probable and suspected EVD cases by week of symptom onset.

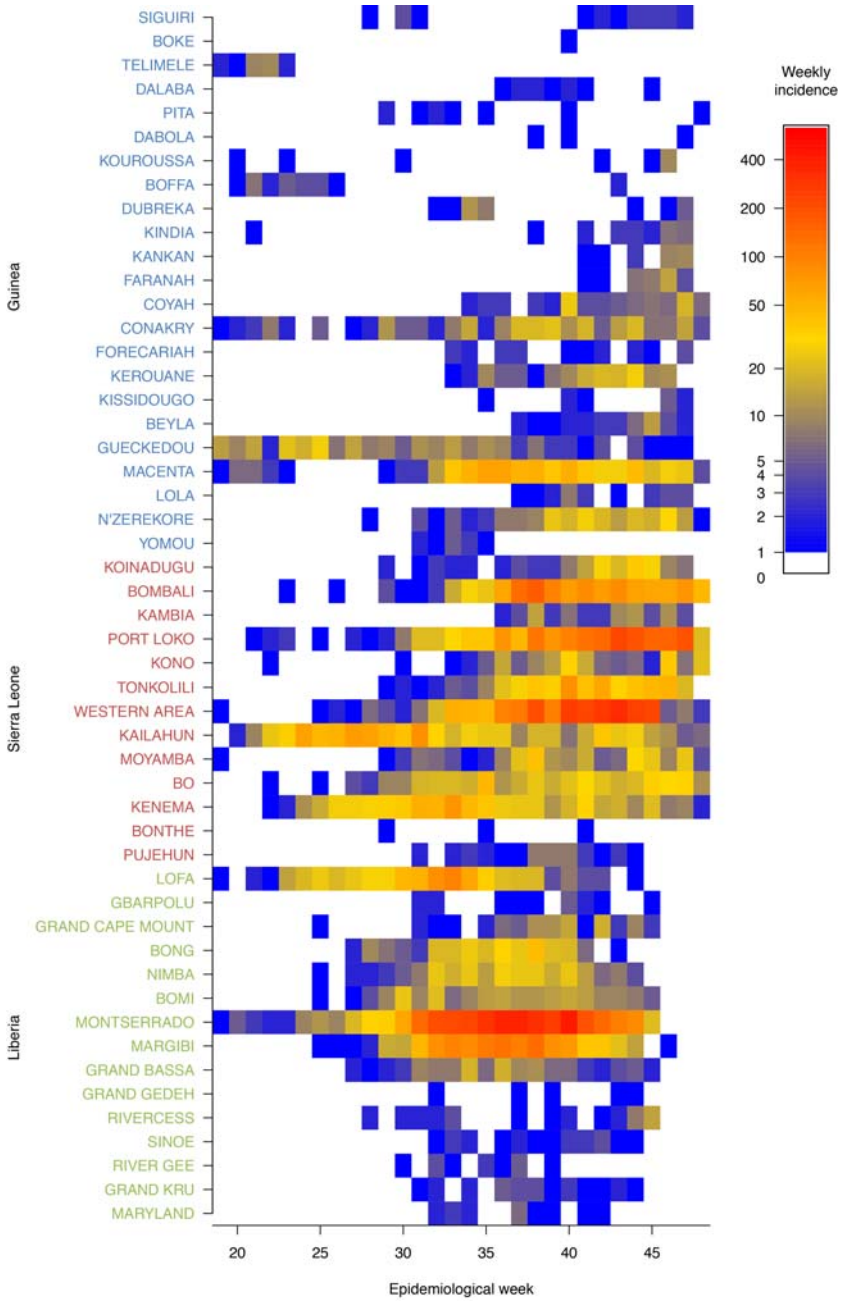

Figure S7(B): As Figure S3(B) for confirmed, probable and suspected EVD cases by week of symptom onset.

Guinea

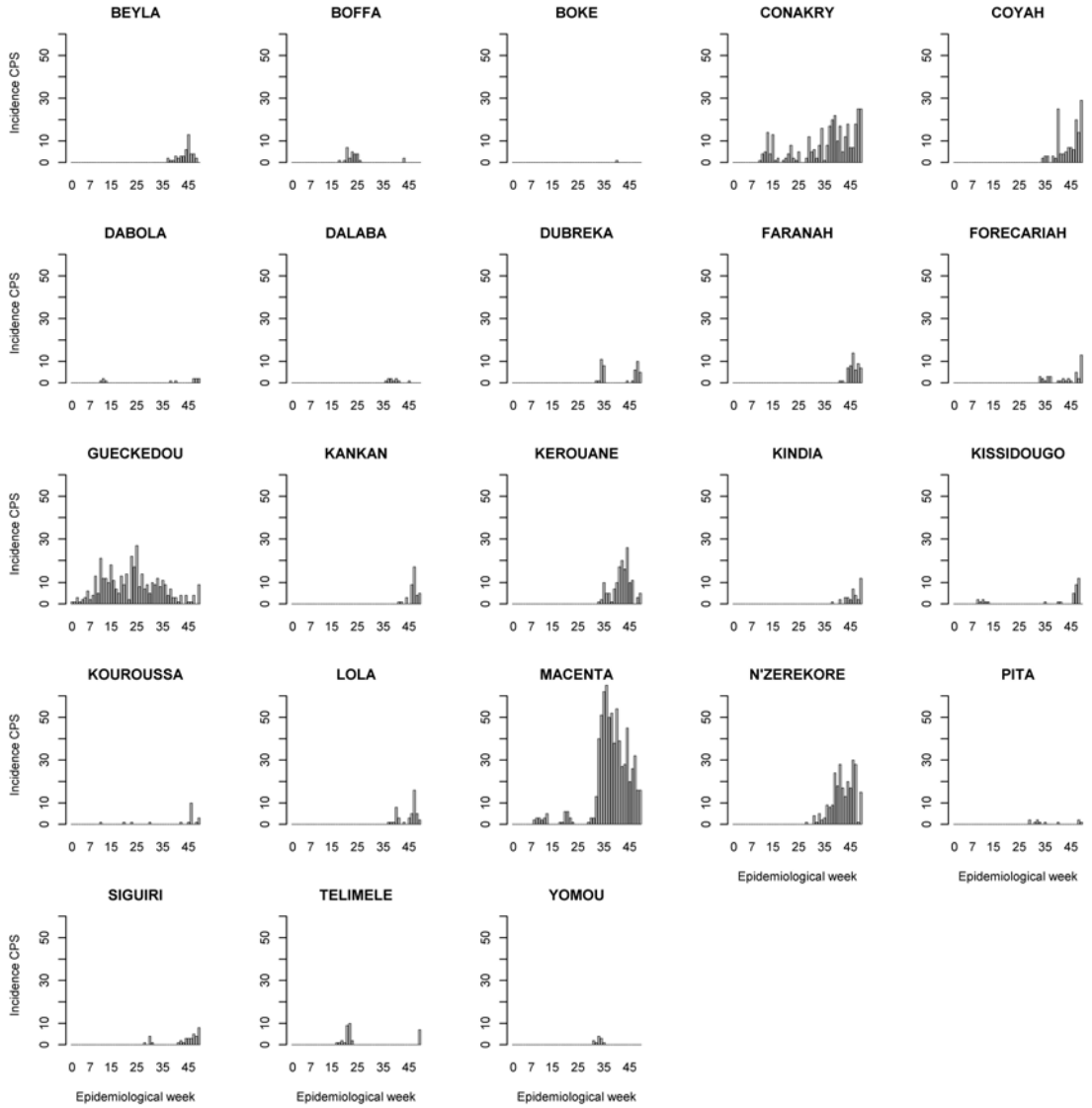

Figure S8: Weekly incidence of confirmed, probable and suspected EVD cases in Guinea by district plotted by week of symptom onset (based on the supplemented daily incidence time series as described in Data Sources, to week starting 1 December 2014). The first day of week 1 for the x-axis is Monday 30 December 2013. Week 20 started on Monday 12 May 2014 and week 40 started on Monday 29 September 2014.

Liberia

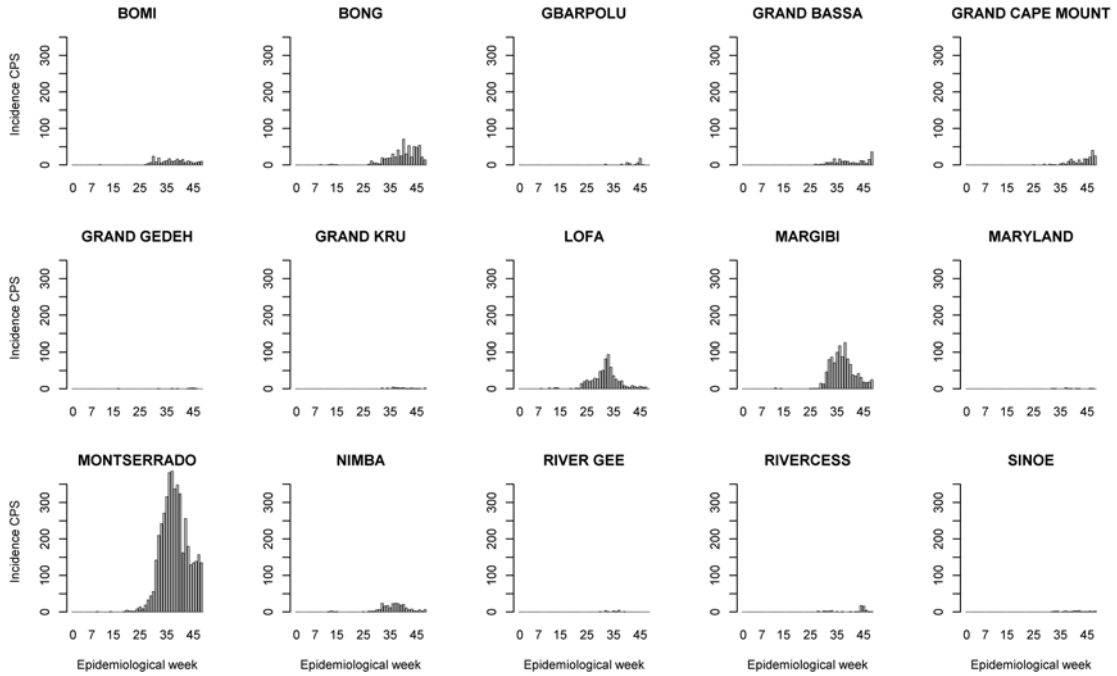

Figure S9: As Figure S8 but for districts in Liberia (to week starting 24 November 2014).

Sierra Leone

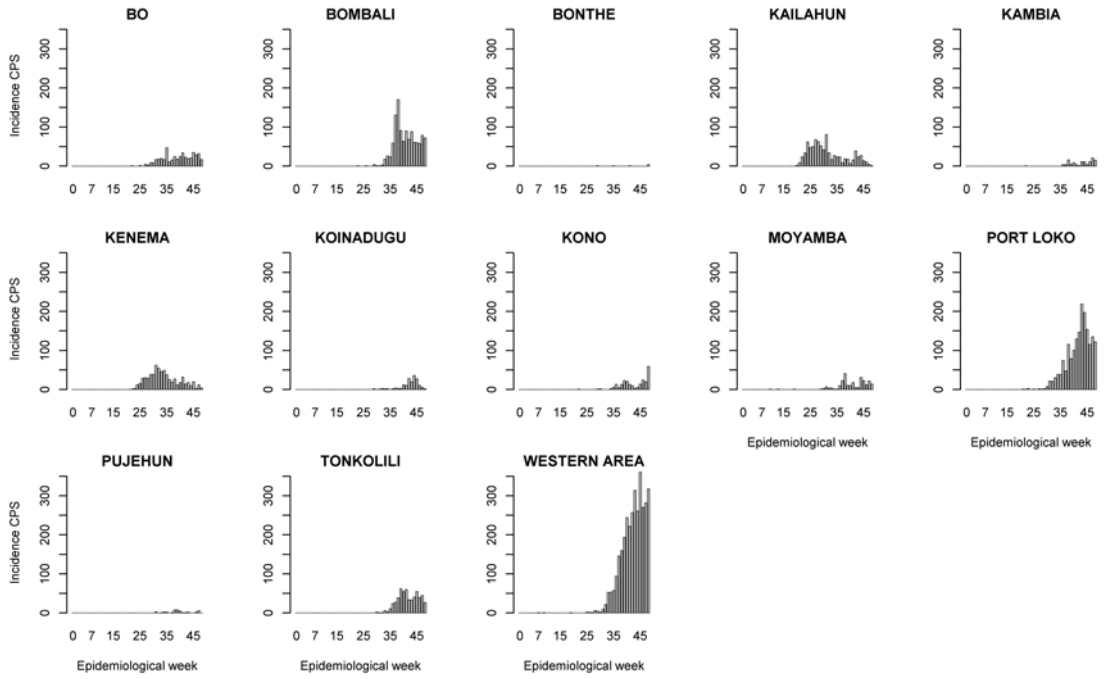

Figure S10: As Figure S8 but for districts in Sierra Leone (to week starting 24 November 2014).

Age distribution of EVD cases

The age distributions of confirmed and probable EVD cases and confirmed, probable and suspected EVD cases are shown in Figures S11 and S12, respectively. The highest number of cases occurred in the 25-34 year old age group, followed by the 35-44 years old. The fewest numbers of cases were < 5 and 65+ years old. Overall, age patterns were similar between countries.

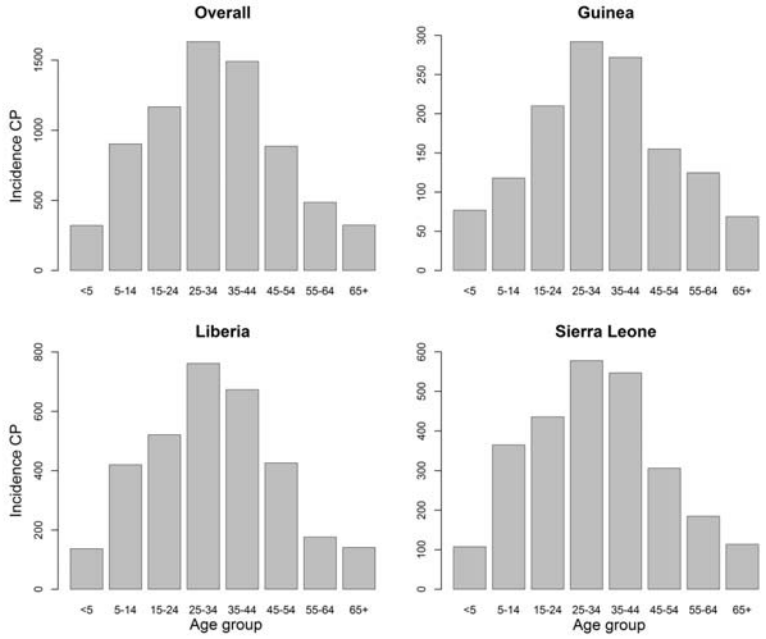

Figure S11: Age distribution of confirmed and probable EVD cases (based on VHF databases).

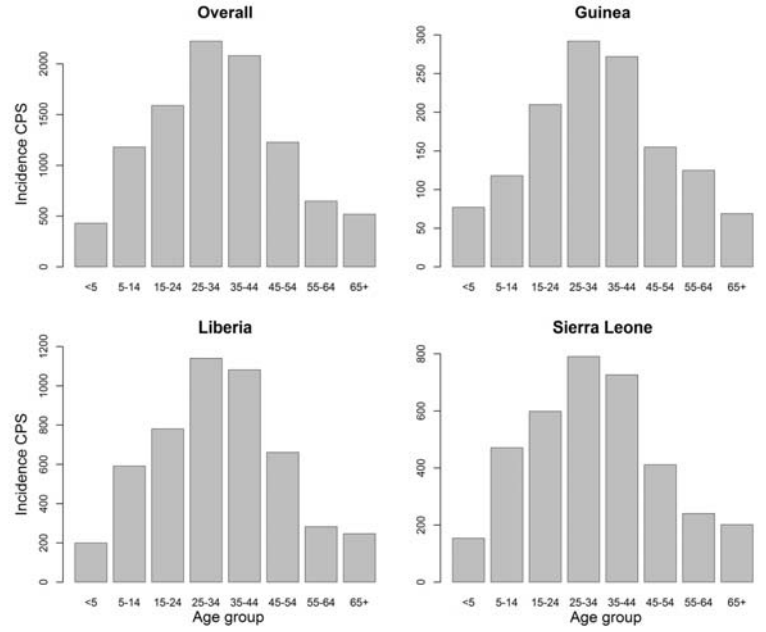

Figure S12: Age distribution of confirmed, probable and suspected EVD cases (based on VHF databases).

Incubation Period

The observed incubation period distribution is shown in Table S1, overall and by country for three time periods: over the course of the EVD epidemic (December 2013 to 25 November 2014 [latest data available at the time of writing]); the early period of the epidemic (December 2013 to 30 September 2014) and the recent period (1 October to 25 November 2014). 1 October coincides with the initiation of the United Nations Mission for Ebola Emergency Response. The median incubation period was 10 days (interquartile range (IQR) 5-15), for the recent time period among confirmed and probable EVD cases. This was similar for confirmed, probable and suspected EVD cases (9 days).

The fitted gamma distributions for incubation period overall and by country are shown in Table S2 and Figures S13-14. Methods used to estimate incubation period have been previously described[1]. The mean incubation period is 1-1.5 days longer, depending on country, for the recent period (1 October to 25 November) compared to the earlier period (Table S2, Figure S15). The fitted mean incubation period during 1 October -25 November among confirmed and probable EVD cases is 11.8 days (95% confidence interval (CI) 11.0-12.7) (for confirmed, probable and suspected EVD cases this is 11.4 days).

Observed Incubation Period

Table S1: Observed Incubation Period Overall and By Country (based on VHF databases)

Observed for Confirmed and Probable EVD Cases Median (IQR, n)			
	Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**
Overall	9 (5, 13; n = 1798)	8 (5, 13; n = 1285)	10 (5, 15; n = 513)
Guinea	9 (4, 17; n = 49)	9 (4, 17; n = 45)	--
Liberia	9 (5, 13; n = 957)	8 (5, 12.5; n = 759)	10 (6, 14; n = 198)
Sierra Leone	9 (5, 13; n = 792)	8 (4, 12; n = 481)	9 (5, 15; n = 311)
Observed for Confirmed, Probable and Suspected EVD Cases Median (IQR, n)			
Overall	9 (5, 13; n = 2118)	8 (5, 13; n = 1494)	9 (5, 14; n = 624)
Guinea	9 (4, 17; n = 49)	9 (4, 17; n = 45)	--
Liberia	9 (5, 13; n = 1080)	8 (5, 12.25; n = 868)	10 (6, 14; n = 212)
Sierra Leone	9 (5, 13; n = 989)	8 (4, 13; n = 581)	9 (5, 14; n = 408)

IQR=Interquartile range, n=sample size; -- not calculated because sample size <10

Fitted Incubation Period

Table S2: Fitted Incubation Period Overall and By Country (based on VHF databases)

Fitted for Confirmed and Probable EVD Cases Estimate (95% CI, n)					
		Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**	**p value**
Overall	Mean	10.3 (9.9 - 10.7; n = 1798)	9.7 (9.2 - 10.1; n = 1285)	11.8 (11.0 - 12.7; n = 513)	<0.001
	SD	8.2 (7.8 - 8.6)	7.6 (7.2 – 8.0)	9.5 (8.7 - 10.5)	<0.001
Guinea	Mean	12.6 (9.1 - 17.1; n = 49)	11.4 (8.5 - 15.1; n = 45)	--	--
	SD	13.1 (9.6 - 19.6)	10.6 (7.8 - 15.6)	--	--
Liberia	Mean	10.0 (9.6 - 10.5; n = 957)	9.6 (9.1 - 10.2; n = 759)	11.6 (10.4 - 12.9; n = 198)	0.003
	SD	7.6 (7.1 - 8.1)	7.2 (6.7 - 7.7)	8.9 (7.8 - 10.4)	0.007
Sierra Leone	Mean	10.4 (9.8 - 11.0; n = 792)	9.5 (8.8 - 10.2; n = 481)	11.8 (10.8 - 12.9; n = 311)	<0.001
	SD	8.6 (8.0 - 9.3)	7.9 (7.2 - 8.8)	9.5 (8.4 - 10.7)	0.014
Fitted for Confirmed, Probable and Suspected EVD Cases Estimate (95% CI, n)					
Overall	Mean	10.3 (10.0 - 10.7; n = 2118)	9.9 (9.5 - 10.3; n = 1494)	11.4 (10.7 - 12.1; n = 624)	<0.001
	SD	8.2 (7.9 - 8.6)	7.7 (7.3 - 8.2)	9.3 (8.6 - 10.1)	<0.001
Guinea	Mean	12.6 (9.1 - 17.1; n = 49)	11.4 (8.5 - 15.1; n = 45)	--	--
	SD	13.1 (9.6 - 19.6)	10.6 (7.8 - 15.6)	--	--
Liberia	Mean	10.1 (9.7 - 10.6; n = 1080)	9.8 (9.3 - 10.3; n = 868)	11.6 (10.5 - 12.9; n = 212)	0.003
	SD	7.7 (7.3 - 8.2)	7.5 (7.0 – 8.0)	8.7 (7.7 - 10.1)	0.03
Sierra Leone	Mean	10.4 (9.8 - 10.9; n = 989)	9.8 (9.2 - 10.5; n = 581)	11.1 (10.2 - 12.0; n = 408)	0.015
	SD	8.5 (8.0 - 9.1)	8.0 (7.3 - 8.7)	9.3 (8.4 - 10.3)	0.018

95% CI = 95% confidence intervals; n= sample size; -- not calculated because sample size <10; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

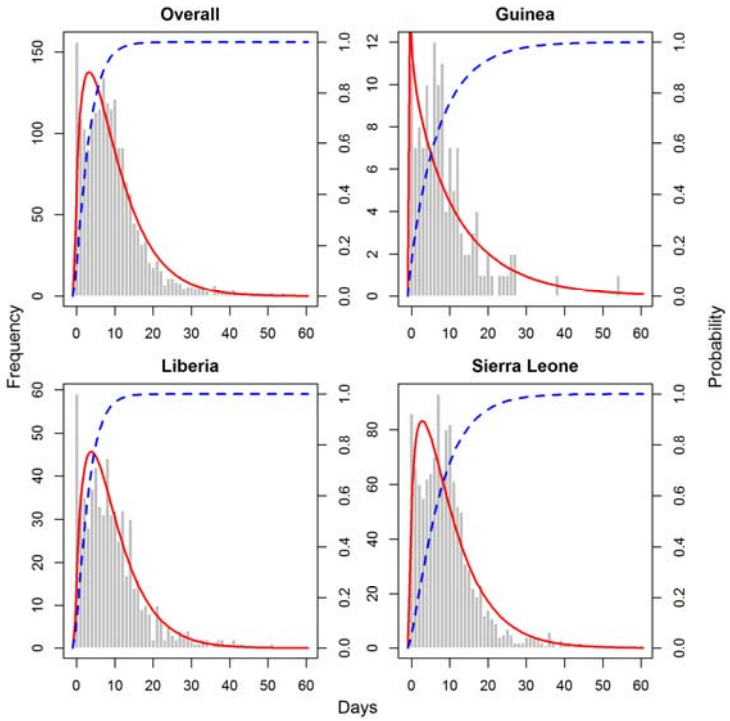

Figure S13: Incubation period distribution for confirmed and probable EVD cases overall and by country (based on VHF databases) including only cases with single day exposure, excluding exposures on day 0 (histograms in grey), best-fit (gamma) probability density function (red curves) and cumulative distribution for the incubation period (blue curve)

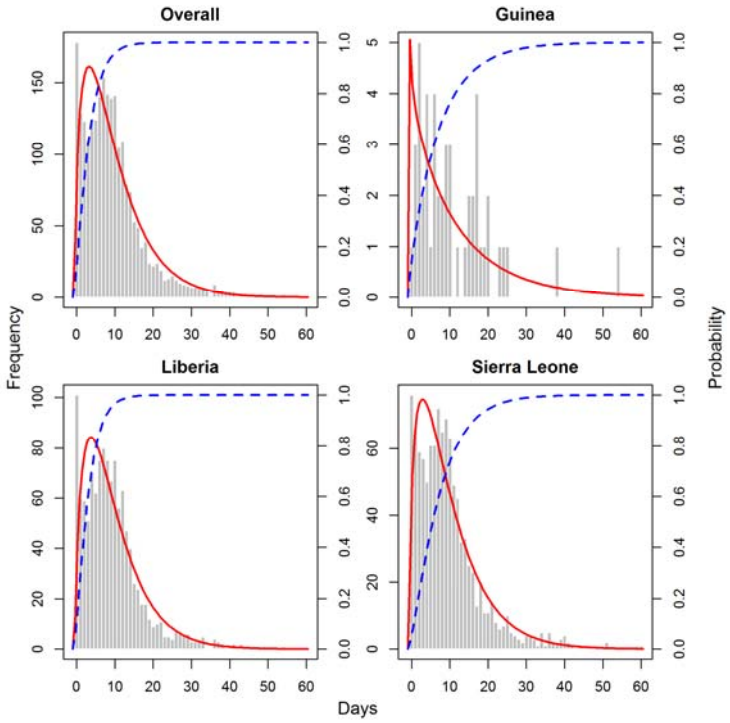

Figure S14: As Figure S13, for confirmed, probable and suspected EVD cases (based on VHF databases)

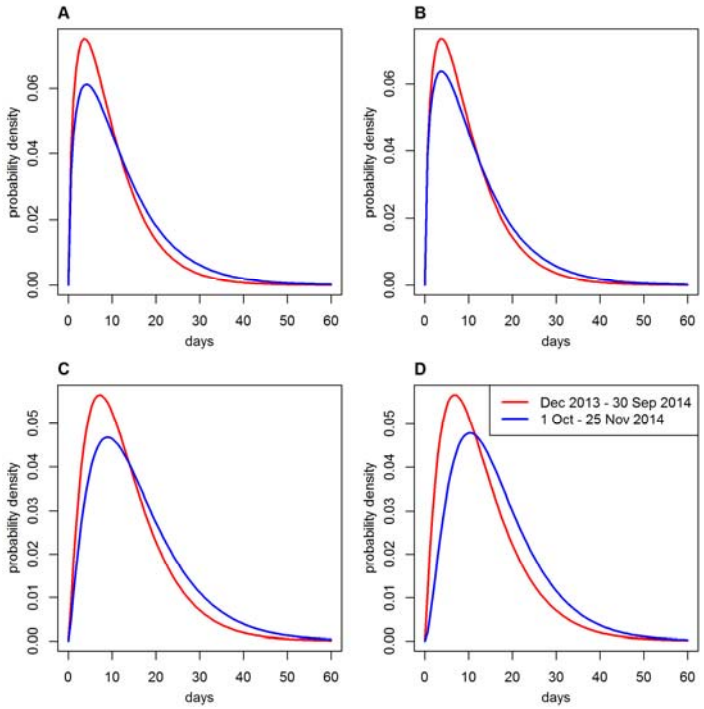

Figure S15: Incubation period distributions (A for confirmed and probable EVD cases; B for confirmed, probable and suspected EVD cases) and serial interval distributions (C for confirmed and probable EVD cases; D for confirmed, probable and suspected EVD cases) prior to and after 1 October 2014 (based on VHF databases)

Serial Interval

The median observed serial intervals overall and by country for the three time periods are shown in Table S3. The mean serial interval (based on the maximum likelihood estimated gamma distribution) overall and by country are shown in Table S3 and Figures S16 and S17. As with the incubation period, the mean fitted serial interval overall and by country is longer during the recent period of the epidemic (1 October to 25 November) compared to the earlier period. Methods used to estimate the serial interval have been previously reported[1].

Observed Serial Interval

Table S3: Observed Serial Interval Overall and By Country (based on VHF databases)

Observed for Confirmed and Probable EVD Cases Median (IQR, n)			
	Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**
Overall*	13 (8, 18; n = 305)	12.5 (8, 17; n = 206)	14 (8, 20; n = 99)
Guinea	15 (10, 19; n = 37)	15 (10, 19; n = 37)	--
Liberia	14 (8, 18; n = 147)	13 (8, 17; n = 104)	16 (8, 31; n = 43)
Sierra Leone	10 (6, 16.25; n = 112)	9 (5, 13.25; n = 56)	13 (8, 17.5; n = 56)
Observed for Confirmed, Probable and Suspected EVD Cases Median (IQR, n)			
Overall*	13 (8, 18; n = 480)	12 (8, 17; n = 328)	15 (10, 20; n = 152)
Guinea	15 (10, 19; n = 37)	15 (10, 19; n = 37)	--
Liberia	14 (9, 18; n = 279)	13 (8, 17; n = 194)	16 (12, 22; n = 85)
Sierra Leone	11 (7, 17; n = 155)	10 (5, 15; n = 88)	14 (8, 18.5; n = 67)

* including Guinea, Liberia, Nigeria and Sierra Leone; IQR=Interquartile range, n=sample size; -- not calculated because sample size <10

Fitted Serial Interval

Table S4: Fitted Serial Interval Overall and By Country (based on VHF databases)

Fitted for Confirmed and Probable EVD Cases Estimate (95% CI, n)					
		Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**	**p value**
Overall*	Mean	14.2 (13.1 - 15.3; n = 305)	13.2 (12.1 - 14.5; n = 206)	16.1 (14.1 - 18.4; n = 99)	0.012
	SD	9.6 (8.6 - 10.7)	8.9 (7.9 - 10.3)	10.7 (9.0 - 13.1)	0.075
Guinea	Mean	15.5 (13.4 - 18.1; n = 37)	15.5 (13.4 - 18.1; n = 37)	--	--
	SD	7.0 (5.5 - 9.4)	7.0 (5.5 - 9.4)	--	--
Liberia	Mean	15.1 (13.5 - 16.9; n = 147)	13.5 (11.9 - 15.5; n = 104)	18.8 (15.4 - 23.3; n = 43)	0.009
	SD	10.5 (9.1 - 12.5)	9.3 (7.8 - 11.4)	12.7 (9.8 - 17.5)	0.057
Sierra Leone	Mean	12.4 (10.8 - 14.2; n = 112)	10.7 (8.6 - 13.3; n = 56)	14.0 (11.9 - 16.6; n = 56)	0.025
	SD	9.0 (7.5 - 10.9)	8.6 (6.6 - 11.7)	8.8 (7.0 - 11.5)	0.45

Fitted for Confirmed, Probable and Suspected EVD Cases Estimate (95% CI, n)					
Overall*	Mean	14.1 (13.3 - 15.0; n = 480)	13.1 (12.1 - 14.1; n = 328)	16.4 (14.9 - 18.1; n = 152)	<0.001
	SD	9.5 (8.8 - 10.4)	9.1 (8.2 - 10.1)	10.0 (8.7 - 11.7)	0.15
Guinea	Mean	15.5 (13.4 - 18.1; n = 37)	15.5 (13.4 - 18.1; n = 37)	--	--
	SD	7.0 (5.5 - 9.4)	7.0 (5.5 - 9.4)	--	--
Liberia	Mean	14.6 (13.5 - 15.9; n = 279)	13.1 (11.9 - 14.5; n = 194)	18.1 (16.1 - 20.4; n = 85)	<0.001
	SD	10.0 (9.0 - 11.3)	9.3 (8.2 - 10.8)	10.1 (8.5 - 12.4)	0.26
Sierra Leone	Mean	12.8 (11.5 - 14.4; n = 155)	11.7 (10.0 - 13.8; n = 88)	14.3 (12.3 - 16.8; n = 67)	0.042
	SD	9.1 (7.9 - 10.8)	8.8 (7.2 - 11.1)	9.2 (7.5 - 11.8)	0.38

*including Guinea, Liberia, Nigeria and Sierra Leone; 95% CI = 95% confidence intervals; n= sample size; -- not calculated because sample size <10; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods.

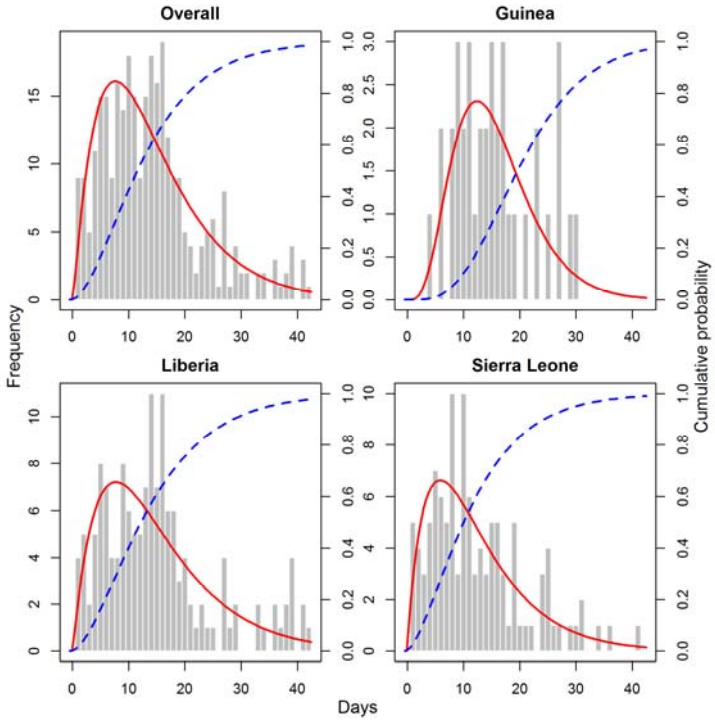

Figure S16: Serial interval distribution for confirmed and probable EVD cases overall and by country (based on VHF databases). Observed times between symptom onsets in an infecting case and the case it infected (histograms in grey) and best-fit (gamma) probability density function (red curve) and cumulative distribution (blue curve) for the serial interval.

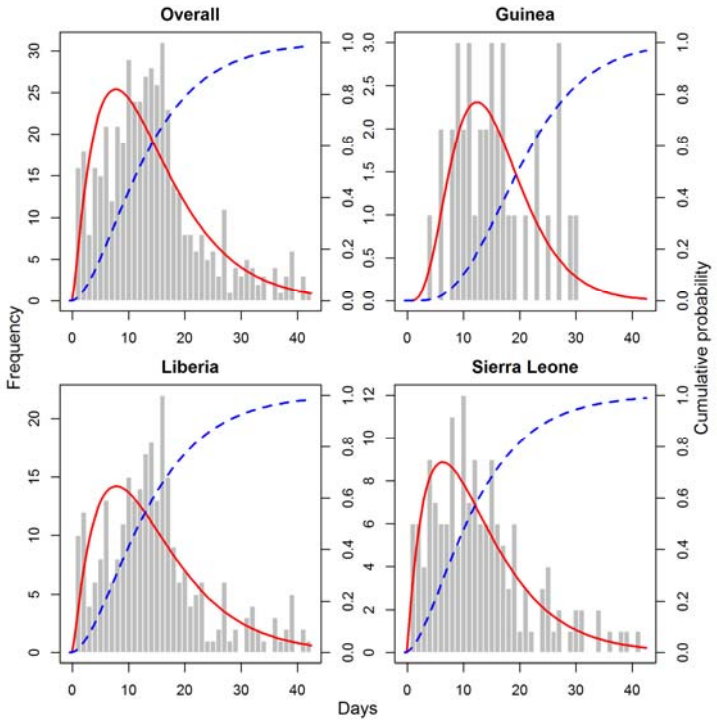

Figure S17: As Figure S16, for confirmed, probable and suspected EVD Cases (based on VHF databases)

Delay Distributions

The observed median time delays between key events in an infected patient's course of illness are shown in Tables S5 and S6. Gamma distributions were fitted to time from:

- symptom onset to hospitalization,
- symptom onset to discharge,
- symptom onset to death,
- symptom onset to notification,
- notification to discharge,
- notification to death,
- hospitalization to discharge and
- hospitalization to death,

and are shown in Tables S7 and S8 for confirmed and probable EVD cases, and confirmed, probable and suspected EVD cases, respectively. Among confirmed and probable EVD cases, the mean fitted time from onset to hospitalization is 4.3 days (95% CI 4.1-4.5 days) for the period 1 October – 25 November 2014, which is a statistically significant reduction in time compared to the time period of December 2013 – 30 September 2014. This reduction is seen for Guinea, Liberia and Sierra Leone individually which would contribute to reduced transmission within the community. The trend is the same when including confirmed, probable and suspected EVD cases (Table S8).

Observed delay distributions

Table S5: Delay Distributions Overall and by Country for Confirmed and Probable EVD cases (based on VHF databases)

	Overall Median (IQR; n)		
Delay	**Dec 2013-25 Nov 2014**	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**
Hospitalization to death	3 (2, 6; n = 1167)	3 (2, 6; n = 930)	3 (2, 5; n = 237)
Hospitalization to discharge	10 (7, 15; n = 1004)	10 (7, 15; n = 813)	11 (7, 14; n = 191)
Notification to death	1 (0, 4; n = 2536)	2 (0, 5; n = 1879)	0 (0, 3; n = 657)
Notification to discharge	10 (6, 15; n = 1324)	10 (6, 15; n = 1080)	10 (6, 13; n = 244)
Onset to death	7 (4, 10; n = 2741)	8 (5, 11; n = 2094)	5 (3, 9; n = 647)
Onset to discharge	15 (9, 20; n = 1335)	15 (9, 20; n = 1085)	15 (10.25, 18; n = 250)
Onset to hospitalization	4 (2, 6; n = 4499)	4 (2, 7; n = 3038)	4 (2, 6; n = 1461)
Onset to notification	4 (2, 7; n = 8672)	4 (2, 7; n = 5820)	4 (2, 6; n = 2852)
	Guinea Median (IQR; n)		
Hospitalization to death	4 (2, 5; n = 488)	3 (2, 5; n = 326)	4 (2, 5; n = 162)
Hospitalization to discharge	11 (8, 14; n = 477)	10 (8, 14; n = 326)	11 (7, 14; n = 151)
Notification to death	3 (0, 5; n = 704)	2 (0, 5; n = 509)	3 (1, 5; n = 195)
Notification to discharge	11 (8, 14; n = 510)	10 (8, 14; n = 344)	11 (7.25, 14; n = 166)
Onset to death	8 (6, 11; n = 693)	8 (6, 11; n = 500)	8 (5, 10; n = 193)
Onset to discharge	16 (12, 20; n = 514)	16 (12, 20; n = 345)	16 (12, 19; n = 169)
Onset to hospitalization	4 (3, 7; n = 1374)	5 (3, 7; n = 818)	4 (3, 6; n = 556)
Onset to notification	5 (3, 7; n = 1885)	5 (3, 8; n = 1192)	4 (3, 6; n = 693)
	Liberia Median (IQR; n)		
Hospitalization to death	3 (1, 5; n = 461)	3 (1, 6; n = 435)	2 (1, 3; n = 26)
Hospitalization to discharge	10 (6.25, 14; n = 214)	10 (6.75, 14; n = 208)	--
Notification to death	1 (0, 4; n = 1017)	1 (0, 4; n = 906)	0 (-1, 2; n = 111)
Notification to discharge	9 (5, 14; n = 247)	9 (5, 14; n = 235)	9 (6.5, 13; n = 12)
Onset to death	8 (5, 11; n = 1292)	8 (5, 11; n = 1173)	4 (3, 8.5; n = 119)
Onset to discharge	15 (10, 20; n = 283)	16 (10, 20; n = 269)	11.5 (7.5, 15.75; n=14)
Onset to hospitalization	5 (2, 7; n = 1315)	5 (3, 7; n = 1148)	3 (1, 5; n = 167)
Onset to notification	5 (2, 7; n = 3026)	5 (2, 7; n = 2481)	3 (2, 6; n = 545)
	Sierra Leone Median (IQR; n)		
Hospitalization to death	4 (2, 6; n = 218)	4 (2, 6; n = 169)	2 (1, 4; n = 49)
Hospitalization to discharge	10 (4, 16; n = 313)	11 (5, 17; n = 279)	7 (3, 12.75; n = 34)
Notification to death	0 (0, 3; n = 815)	2 (0, 5; n = 464)	0 (-1, 0; n = 351)
Notification to discharge	9 (4, 16; n = 567)	10 (4, 17; n = 501)	5.5 (3, 12; n = 66)
Onset to death	5 (3, 8; n = 756)	7 (3, 9; n = 421)	4 (2, 6; n = 335)
Onset to discharge	12.5 (6, 20; n = 538)	13 (7, 21; n = 471)	9 (5, 15; n = 67)
Onset to hospitalization	3.5 (2, 5; n = 1810)	3 (2, 5; n = 1072)	4 (2, 5; n = 738)
Onset to notification	3 (2, 6; n = 3761)	3 (1, 5; n = 2147)	4 (2, 6; n = 1614)

*Including cases reported as of 25 November 2014; IQR = interquartile range, n=sample size; -- not calculated because sample size <10

Table S6: As Table S5, for Confirmed, Probable and Suspected EVD cases (based on VHF databases)

Delay	Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014
	Overall Median (IQR; n)		
Hospitalization to death	3 (1, 5; n = 1325)	3 (1, 6; n = 1055)	3 (1, 5; n = 270)
Hospitalization to discharge	10 (7, 14; n = 1084)	10 (6, 15; n = 884)	10 (7, 14; n = 200)
Notification to death	0 (0, 3; n = 3807)	0 (0, 4; n = 2658)	0 (-1, 1; n = 1149)
Notification to discharge	10 (5, 14; n = 1438)	10 (5, 15; n = 1170)	9 (5, 13; n = 268)
Onset to death	7 (3, 10; n = 4073)	8 (4, 11; n = 2964)	4 (2, 8; n = 1109)
Onset to discharge	14 (9, 19; n = 1457)	14 (9, 20; n = 1183)	14 (9, 18; n = 274)
Onset to hospitalization	4 (2, 6; n = 5302)	4 (2, 7; n = 3553)	4 (2, 6; n = 1749)
Onset to notification	4 (2, 7; n = 12143)	4 (2, 7; n = 7835)	4 (2, 6; n = 4308)
	Guinea Median (IQR; n)		
Hospitalization to death	4 (2, 5; n = 488)	3 (2, 5; n = 326)	4 (2, 5; n = 162)
Hospitalization to discharge	11 (8, 14; n = 479)	10 (8, 14; n = 326)	11 (7, 14; n = 153)
Notification to death	3 (0, 5; n = 704)	2 (0, 5; n = 509)	3 (1, 5; n = 195)
Notification to discharge	11 (8, 14; n = 512)	10 (8, 14; n = 344)	11 (7, 14; n = 168)
Onset to death	8 (6, 11; n = 693)	8 (6, 11; n = 500)	8 (5, 10; n = 193)
Onset to discharge	16 (12, 20; n = 516)	16 (12, 20; n = 345)	16 (12, 19; n = 171)
Onset to hospitalization	4 (3, 7; n = 1422)	5 (3, 7; n = 818)	4 (2, 6; n = 604)
Onset to notification	5 (3, 7; n = 1935)	5 (3, 8; n = 1192)	4 (3, 6; n = 743)
	Liberia Median (IQR; n)		
Hospitalization to death	3 (1, 5; n = 579)	3 (1, 5; n = 540)	2 (1, 3; n = 39)
Hospitalization to discharge	9 (5, 13; n = 276)	9 (5, 13; n = 268)	--
Notification to death	0 (-1, 3; n = 1773)	0 (0, 3; n = 1484)	0 (-1, 0; n = 289)
Notification to discharge	9 (5, 13; n = 312)	9 (5, 13; n = 297)	9 (5, 12; n = 15)
Onset to death	8 (4, 11; n = 2153)	8 (5, 11; n = 1853)	4 (2, 8; n = 300)
Onset to discharge	14 (8, 19; n = 357)	14 (8, 19; n = 340)	11 (7, 16; n = 17)
Onset to hospitalization	4.5 (2, 7; n = 1746)	5 (2.5, 7; n = 1495)	3 (1, 6; n = 251)
Onset to notification	5 (2, 8; n = 4928)	5 (3, 8; n = 3872)	4 (2, 7; n = 1056)
	Sierra Leone Median (IQR; n)		
Hospitalization to death	3 (1, 6; n = 258)	4 (2, 6; n = 189)	2 (1, 4; n = 69)
Hospitalization to discharge	10 (4, 16; n = 329)	10.5 (5, 17; n = 290)	5 (2.5, 11.5; n = 39)
Notification to death	0 (-1, 2; n = 1330)	1 (0, 4; n = 665)	0 (-1, 0; n = 665)
Notification to discharge	8 (3, 16; n = 614)	9 (3, 17; n = 529)	4 (2, 10; n = 85)
Onset to death	4 (2, 8; n = 1227)	5 (3, 9; n = 611)	3 (1, 6; n = 616)
Onset to discharge	11 (5, 20; n = 584)	12 (6, 20; n = 498)	7 (4.3, 13.8; n = 86)
Onset to hospitalization	3 (2, 5; n = 2134)	3 (2, 5; n = 1240)	4 (2, 5; n = 894)
Onset to notification	4 (2, 6; n = 5280)	3 (1, 5; n = 2771)	4 (2, 6; n = 2509)

IQR = interquartile range, n=sample size; -- not calculated because sample size <10

Fitted delay distributions

Table S7: Fitted Delay Distributions among Confirmed and Probable EVD cases overall and by country (based on VHF databases)

		Overall (estimate [95% CI; n])			
		Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**	**p value**
Hospitalization to death	mean	4.3 (4.1 - 4.5; n = 1167)	4.4 (4.2 - 4.7; n = 930)	3.8 (3.4 - 4.3; n = 237)	0.01
	sd	4.0 (3.8 - 4.3)	4.2 (3.9 - 4.5)	3.3 (2.9 - 3.8)	0.001
Hospitalization to discharge	mean	11.2 (10.8 - 11.7; n = 1004)	11.4 (10.9 - 11.9; n = 813)	10.6 (9.7 - 11.5; n = 191)	0.068
	sd	7.2 (6.8 - 7.6)	7.4 (7 - 7.9)	6.2 (5.5 - 7.1)	0.005
Notification to death	mean	3.5 (3.3 - 3.7; n = 2536)	3.9 (3.7 - 4.2; n = 1879)	2.2 (1.9 - 2.5; n = 657)	<0.001
	sd	5.0 (4.7 - 5.4)	5.3 (4.9 - 5.7)	3.6 (3.1 - 4.3)	<0.001
Notification to discharge	mean	10.9 (10.5 - 11.4; n = 1324)	11.2 (10.7 - 11.7; n = 1080)	9.9 (9.1 - 10.7; n = 244)	0.003
	sd	8.2 (7.8 - 8.7)	8.6 (8.1 - 9.2)	6.3 (5.6 - 7.1)	<0.001
Onset to death	mean	8.2 (7.9 - 8.4; n = 2741)	8.8 (8.5 - 9.1; n = 2094)	6.2 (5.8 - 6.6; n = 647)	<0.001
	sd	6.4 (6.1 - 6.6)	6.5 (6.2 - 6.8)	5.3 (4.9 - 5.8)	<0.001
Onset to discharge	mean	15.1 (14.6 - 15.6; n = 1335)	15.3 (14.7 - 15.8; n = 1085)	14.4 (13.5 - 15.4; n = 250)	0.063
	sd	8.9 (8.5 - 9.3)	9.2 (8.8 - 9.7)	7.4 (6.7 - 8.3)	<0.001
Onset to hospitalization	mean	5 (4.9 - 5.1; n = 4499)	5.3 (5.1 - 5.5; n = 3038)	4.3 (4.1 - 4.5; n = 1461)	<0.001
	sd	4.4 (4.3 - 4.6)	4.7 (4.6 - 4.9)	3.7 (3.5 – 4.0)	<0.001
Onset to notification	mean	5.5 (5.4 - 5.7; n = 8672)	5.9 (5.7 - 6.0; n = 5820)	4.9 (4.7 - 5.0; n = 2852)	<0.001
	sd	5.2 (5.1 - 5.3)	5.8 (5.6 - 5.9)	4.0 (3.8 - 4.2)	<0.001
		Guinea (estimate [95% CI; n])			
Hospitalization to death	mean	4.3 (4 - 4.6; n = 488)	4.2 (3.8 - 4.6; n = 326)	4.4 (3.9 - 5.0; n = 162)	0.30
	sd	3.6 (3.3 - 3.9)	3.6 (3.2 – 4.0)	3.6 (3.0 - 4.2)	0.49
Hospitalization to discharge	mean	11.1 (10.7 - 11.6; n = 477)	11.1 (10.5 - 11.7; n = 326)	11.2 (10.4 - 12.1; n = 151)	0.40
	sd	5.5 (5.1 - 5.9)	5.6 (5.1 - 6.2)	5.2 (4.6 - 6.0)	0.20
Notification to death	mean	3.7 (3.4 - 4.1; n = 704)	3.6 (3.3 - 4.1; n = 509)	3.9 (3.4 - 4.5; n = 195)	0.21
	sd	4.1 (3.7 - 4.5)	4.2 (3.7 - 4.8)	3.7 (3.1 - 4.4)	0.11
Notification to discharge	mean	11.1 (10.6 - 11.6; n = 510)	11.2 (10.6 - 11.9; n = 344)	10.8 (9.9 - 11.7; n = 166)	0.21
	sd	5.8 (5.4 - 6.3)	5.8 (5.3 - 6.4)	5.8 (5.1 - 6.7)	0.48
Onset to death	mean	8.4 (8.0 - 8.8; n = 693)	8.6 (8.2 - 9.1; n = 500)	7.9 (7.1 - 8.8; n = 193)	0.054
	sd	5.3 (5.0 - 5.7)	5.1 (4.7 - 5.5)	5.9 (5.1 - 6.9)	0.043
Onset to discharge	mean	16.3 (15.8 - 16.9; n = 514)	16.5 (15.8 - 17.1; n = 345)	16.1 (15.1 - 17.1; n = 169)	0.26
	sd	6.3 (5.9 - 6.8)	6.3 (5.8 - 6.9)	6.4 (5.7 - 7.2)	0.43
Onset to hospitalization	mean	5.2 (5.0 - 5.4; n = 1374)	5.4 (5.1 - 5.7; n = 818)	4.8 (4.5 - 5.1; n = 556)	0.001
	sd	4.0 (3.8 - 4.2)	4.2 (3.9 - 4.5)	3.6 (3.3 - 3.9)	0.002
Onset to notification	mean	6.3 (6.1 - 6.5; n = 1885)	7.0 (6.7 - 7.4; n = 1192)	5.0 (4.7 - 5.3; n = 693)	<0.001
	sd	5.3 (5.1 - 5.6)	6.2 (5.9 - 6.7)	3.6 (3.3 - 3.9)	<0.001

Table continued on next page

		Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
		Liberia (estimate [95% CI; n])			
Hospitalization to death	mean	3.9 (3.6 - 4.3; n = 461)	4.0 (3.7 - 4.4; n = 435)	2.7 (2.0 - 3.8; n = 26)	0.005
	sd	3.8 (3.4 - 4.3)	3.9 (3.5 - 4.4)	2.1 (1.5 - 3.4)	0.001
Hospitalization to discharge	mean	10.9 (9.9 - 12.0; n = 214)	10.9 (9.9 - 12.0; n = 208)	--	--
	sd	7.7 (6.8 - 8.8)	7.6 (6.7 - 8.7)	--	--
Notification to death	mean	3.4 (3.1 - 3.8; n = 1017)	3.6 (3.2 - 4.0; n = 906)	1.9 (1.4 - 2.7; n = 111)	<0.001
	sd	5.1 (4.6 - 5.8)	5.3 (4.7 - 6.0)	2.8 (2.0 - 4.2)	<0.001
Notification to discharge	mean	10.6 (9.7 - 11.6; n = 247)	10.6 (9.7 - 11.6; n = 235)	10.6 (7.7 - 15.0; n = 12)	0.50
	sd	7.4 (6.6 - 8.4)	7.5 (6.7 - 8.6)	5.7 (3.8 - 10.4)	0.15
Onset to death	mean	8.8 (8.5 - 9.2; n = 1292)	9.1 (8.8 - 9.5; n = 1173)	5.8 (5.1 - 6.7; n = 119)	<0.001
	sd	6.7 (6.3 - 7.1)	6.8 (6.4 - 7.2)	4.5 (3.8 - 5.5)	<0.001
Onset to discharge	mean	15.7 (14.8 - 16.6; n = 283)	15.8 (14.9 - 16.7; n = 269)	13.6 (10.3 - 18.7; n = 14)	0.17
	sd	7.6 (6.9 - 8.4)	7.6 (6.9 - 8.4)	7.3 (4.9 - 12.6)	0.43
Onset to hospitalization	mean	5.7 (5.4 - 6.0; n = 1315)	6.0 (5.7 - 6.4; n = 1148)	3.3 (2.8 - 3.9; n = 167)	<0.001
	sd	5.5 (5.2 - 5.9)	5.7 (5.3 - 6.1)	3.5 (2.9 - 4.3)	<0.001
Onset to notification	mean	6.1 (5.9 - 6.3; n = 3026)	6.5 (6.2 - 6.7; n = 2481)	4.3 (4.0 - 4.6; n = 545)	<0.001
	sd	5.9 (5.7 - 6.2)	6.3 (6.0 - 6.6)	3.9 (3.5 - 4.3)	<0.001
		Sierra Leone (estimate [95% CI; n])			
Hospitalization to death	mean	5.2 (4.5 - 6.0; n = 218)	5.9 (5.1 - 6.9; n = 169)	2.6 (2 - 3.4; n = 49)	<0.001
	sd	5.3 (4.5 - 6.3)	5.9 (5.0 - 7.1)	2.4 (1.8 - 3.4)	<0.001
Hospitalization to discharge	mean	11.6 (10.6 - 12.6; n = 313)	12.0 (11.0 - 13.1; n = 279)	7.9 (6 - 10.6; n = 34)	0.001
	sd	9.0 (8.0 - 10.1)	9.1 (8.2 - 10.3)	6.5 (4.7 - 9.7)	0.029
Notification to death	mean	3.3 (2.9 - 3.8; n = 815)	4.8 (4.2 - 5.4; n = 464)	0.9 (0.7 - 1.3; n = 351)	<0.001
	sd	5.7 (5.0 - 6.6)	6.2 (5.4 - 7.2)	2.4 (1.8 - 3.6)	<0.001
Notification to discharge	mean	11.0 (10.2 - 11.8; n = 567)	11.4 (10.5 - 12.4; n = 501)	7.5 (6.2 - 9.1; n = 66)	<0.001
	sd	10.1 (9.2 - 11.1)	10.6 (9.7 - 11.8)	5.8 (4.6 - 7.6)	<0.001
Onset to death	mean	6.8 (6.4 - 7.3; n = 756)	8.0 (7.4 - 8.7; n = 421)	5.3 (4.8 - 5.9; n = 335)	<0.001
	sd	6.1 (5.7 - 6.6)	6.8 (6.2 - 7.6)	4.8 (4.3 - 5.5)	<0.001
Onset to discharge	mean	13.7 (12.8 - 14.6; n = 538)	14.1 (13.2 - 15.1; n = 471)	10.4 (9.0 - 12.2; n = 67)	<0.001
	sd	10.3 (9.5 - 11.3)	10.8 (9.9 - 11.9)	6.7 (5.4 - 8.5)	<0.001
Onset to hospitalization	mean	4.3 (4.2 - 4.5; n = 1810)	4.5 (4.2 - 4.7; n = 1072)	4.2 (3.9 - 4.5; n = 738)	0.077
	sd	3.9 (3.7 - 4.2)	4.0 (3.8 - 4.3)	3.8 (3.5 - 4.1)	0.10
Onset to notification	mean	4.8 (4.6 - 4.9; n = 3761)	4.6 (4.4 - 4.8; n = 2147)	5.0 (4.8 - 5.2; n = 1614)	0.002
	sd	4.4 (4.3 - 4.6)	4.5 (4.3 - 4.8)	4.2 (4.0 - 4.4)	0.017

IQR = interquartile range, n=sample size, (95% CI); sd= standard deviation; -- not calculated because sample size <10; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Table S8: As Table S7, for Confirmed, Probable and Suspected EVD cases (based on VHF databases)

		Overall (estimate [95% CI; n])			
		Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**	**p value**
Hospitalization to death	mean	4.3 (4.1- 4.5; n = 1325)	4.5 (4.2 - 4.7; n = 1055)	3.7 (3.3 - 4.1; n = 270)	0.001
	sd	4.2 (4.0 - 4.5)	4.4 (4.1 - 4.8)	3.4 (3.0 - 3.9)	<0.001
Hospitalization to discharge	mean	10.9 (10.5 - 11.4; n = 1084)	11.1 (10.6 - 11.6; n = 884)	10.3 (9.4 - 11.2; n = 200)	0.073
	sd	7.4 (7.0 - 7.8)	7.6 (7.1 - 8.1)	6.5 (5.7 - 7.4)	0.011
Notification to death	mean	3.0 (2.8 - 3.2; n = 3807)	3.5 (3.3 - 3.7; n = 2658)	1.7 (1.4 - 2.0; n = 1149)	<0.001
	sd	5.2 (4.9 - 5.6)	5.6 (5.2 - 6.0)	3.7 (3.1 - 4.4)	<0.001
Notification to discharge	mean	10.5 (10.1 - 11.0; n = 1438)	10.8 (10.3 - 11.3; n = 1170)	9.2 (8.4 - 10.1; n = 268)	<0.001
	sd	8.4 (7.9 - 8.8)	8.7 (8.2 - 9.3)	6.7 (6.0 - 7.6)	<0.001
Onset to death	mean	7.9 (7.7 - 8.1; n = 4073)	8.7 (8.5 - 9.0; n = 2964)	5.6 (5.3 - 5.9; n = 1109)	<0.001
	sd	6.8 (6.6 - 7.0)	7.0 (6.7 - 7.2)	5.4 (5.0 - 5.8)	<0.001
Onset to discharge	mean	14.7 (14.2 - 15.1; n = 1457)	14.9 (14.4 - 15.4; n = 1183)	13.7 (12.8 - 14.7; n = 274)	0.017
	sd	9.0 (8.6 - 9.5)	9.3 (8.8 - 9.8)	7.7 (7.0 - 8.6)	0.001
Onset to hospitalization	mean	4.9 (4.8 - 5.0; n = 5302)	5.2 (5.1 - 5.4; n = 3553)	4.2 (4.1 - 4.4; n = 1749)	<0.001
	sd	4.5 (4.3 - 4.6)	4.8 (4.6 - 5.0)	3.7 (3.5 - 3.9)	<0.001
Onset to notification	mean	5.9 (5.8 - 6.0; n = 12143)	6.4 (6.2 - 6.5; n = 7835)	5.0 (4.9 - 5.1; n = 4308)	<0.001
	sd	5.6 (5.5 - 5.7)	6.4 (6.2 - 6.5)	4.2 (4.0 - 4.3)	<0.001
		Guinea (estimate [95% CI; n])			
Hospitalization to death	mean	4.3 (4.0 - 4.6; n = 488)	4.2 (3.8 - 4.6; n = 326)	4.4 (3.9 - 5.0; n = 162)	0.30
	sd	3.6 (3.3 - 3.9)	3.6 (3.2 - 4.0)	3.6 (3.0 - 4.2)	0.49
Hospitalization to discharge	mean	11.1 (10.6 - 11.6; n = 479)	11.1 (10.5 - 11.7; n = 326)	11.2 (10.4 - 12.0; n = 153)	0.45
	sd	5.5 (5.1 - 5.9)	5.6 (5.1 - 6.2)	5.2 (4.6 - 6.0)	0.22
Notification to death	mean	3.7 (3.4 - 4.1; n = 704)	3.6 (3.3 - 4.1; n = 509)	3.9 (3.4 - 4.5; n = 195)	0.21
	sd	4.1 (3.7 - 4.5)	4.2 (3.7 - 4.8)	3.7 (3.1 - 4.4)	0.11
Notification to discharge	mean	11.1 (10.6 - 11.6; n = 512)	11.2 (10.6 - 11.9; n = 344)	10.7 (9.9 - 11.7; n = 168)	0.18
	sd	5.8 (5.4 - 6.3)	5.8 (5.3 - 6.4)	5.8 (5.1 - 6.7)	0.49
Onset to death	mean	8.4 (8.0 - 8.8; n = 693)	8.6 (8.2 - 9.1; n = 500)	7.9 (7.1 - 8.8; n = 193)	0.054
	sd	5.3 (5.0 - 5.7)	5.1 (4.7 - 5.5)	5.9 (5.1 - 6.9)	0.043
Onset to discharge	mean	16.3 (15.8 - 16.9; n = 516)	16.5 (15.8 - 17.1; n = 345)	16.0 (15.1 - 17.0; n = 171)	0.22
	sd	6.4 (5.9 - 6.8)	6.3 (5.8 - 6.9)	6.5 (5.8 - 7.3)	0.36
Onset to hospitalization	mean	5.1 (4.9 - 5.3; n = 1422)	5.4 (5.1 - 5.7; n = 818)	4.7 (4.4 - 5.0; n = 604)	<0.001
	sd	4.0 (3.8 - 4.2)	4.2 (3.9 - 4.5)	3.6 (3.3 - 3.9)	0.002
Onset to notification	mean	6.2 (6.0 - 6.5; n = 1935)	7.0 (6.7 - 7.4; n = 1192)	4.9 (4.6 - 5.2; n = 743)	<0.001
	sd	5.3 (5.0 - 5.5)	6.2 (5.9 - 6.7)	3.6 (3.3 - 3.9)	<0.001

Table continued on next page

		Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
		Liberia (estimate [95% CI; n])			
Hospitalization to death	mean	4.0 (3.7 - 4.4; n = 579)	4.1 (3.8 - 4.5; n = 540)	2.5 (1.9 - 3.3; n = 39)	<0.001
	sd	4.2 (3.8 - 4.7)	4.4 (3.9 - 4.9)	2.2 (1.6 - 3.2)	<0.001
Hospitalization to discharge	mean	9.9 (9.1 - 10.9; n = 276)	10.0 (9.1 - 11.0; n = 268)	--	--
	sd	7.7 (6.9 - 8.8)	7.7 (6.8 - 8.7)	--	--
Notification to death	mean	2.9 (2.7 - 3.2; n = 1773)	3.2 (2.9 - 3.6; n = 1484)	1.0 (0.7 - 1.5; n = 289)	<0.001
	sd	5.4 (4.9 - 6.1)	5.7 (5.1 - 6.4)	2.3 (1.6 - 3.5)	<0.001
Notification to discharge	mean	9.8 (9.0 - 10.7; n = 312)	9.8 (9.0 - 10.7; n = 297)	9.3 (6.4 - 14.4; n = 15)	0.40
	sd	7.4 (6.6 - 8.3)	7.4 (6.6 - 8.4)	7.0 (4.5 - 13.1)	0.43
Onset to death	mean	8.6 (8.3 - 8.9; n = 2153)	9.1 (8.7 - 9.4; n = 1853)	5.6 (5.1 - 6.2; n = 300)	<0.001
	sd	7.0 (6.7 - 7.3)	7.2 (6.8 - 7.5)	4.7 (4.2 - 5.3)	<0.001
Onset to discharge	mean	14.7 (13.9 - 15.6; n = 357)	14.8 (14.0 - 15.7; n = 340)	12.8 (9.8 - 17.2; n = 17)	0.15
	sd	7.9 (7.2 - 8.6)	7.9 (7.2 - 8.7)	7.1 (5.0 - 11.7)	0.34
Onset to hospitalization	mean	5.6 (5.3 - 5.8; n = 1746)	5.9 (5.6 - 6.1; n = 1495)	4.0 (3.5 - 4.5; n = 251)	<0.001
	sd	5.3 (5.1 - 5.7)	5.5 (5.2 - 5.9)	3.9 (3.4 - 4.6)	<0.001
Onset to notification	mean	6.7 (6.5 - 6.9; n = 4928)	7.1 (6.9 - 7.4; n = 3872)	5.0 (4.7 - 5.3; n = 1056)	<0.001
	sd	6.5 (6.3 - 6.7)	7.1 (6.8 - 7.4)	4.3 (4.0 - 4.6)	<0.001
		Sierra Leone (estimate [95% CI; n])			
Hospitalization to death	mean	5.0 (4.4 - 5.7; n = 258)	5.8 (5.0 - 6.7; n = 189)	2.8 (2.2 - 3.6; n = 69)	<0.001
	sd	5.4 (4.6 - 6.3)	5.9 (5.0 - 7.1)	3.0 (2.2 - 4.1)	<0.001
Hospitalization to discharge	mean	11.4 (10.5 - 12.5; n = 329)	12.0 (11.0 - 13.1; n = 290)	7.2 (5.5 - 9.7; n = 39)	<0.001
	sd	9.1 (8.2 - 10.2)	9.2 (8.2 - 10.4)	6.4 (4.7 - 9.5)	0.019
Notification to death	mean	2.6 (2.3 - 3.0; n = 1330)	3.9 (3.4 - 4.5; n = 665)	0.9 (0.7 - 1.3; n = 665)	<0.001
	sd	5.8 (5.0 - 6.7)	6.5 (5.6 - 7.6)	3.2 (2.3 - 4.7)	<0.001
Notification to discharge	mean	10.4 (9.6 - 11.3; n = 614)	11.1 (10.2 - 12.1; n = 529)	6.2 (5.1 - 7.6; n = 85)	<0.001
	sd	10.2 (9.3 - 11.3)	10.8 (9.8 - 12.0)	5.6 (4.5 - 7.2)	<0.001
Onset to death	mean	6.3 (5.9 - 6.7; n = 1227)	7.8 (7.2 - 8.4; n = 611)	4.8 (4.5 - 5.3; n = 616)	<0.001
	sd	6.4 (6.0 - 6.9)	7.4 (6.7 - 8.1)	5.1 (4.6 - 5.6)	<0.001
Onset to discharge	mean	13.1 (12.3 - 14.0; n = 584)	13.8 (12.9 - 14.8; n = 498)	9.4 (8.1 - 10.8; n = 86)	<0.001
	sd	10.3 (9.5 - 11.2)	10.9 (10.0 - 11.9)	6.3 (5.2 - 7.8)	<0.001
Onset to hospitalization	mean	4.2 (4.1 - 4.4; n = 2134)	4.4 (4.2 - 4.6; n = 1240)	4.0 (3.8 - 4.3; n = 894)	0.013
	sd	4.0 (3.8 - 4.2)	4.2 (3.9 - 4.4)	3.7 (3.4 - 4.0)	0.008
Onset to notification	mean	5.0 (4.9 - 5.1; n = 5280)	5.0 (4.8 - 5.2; n = 2771)	5.0 (4.8 - 5.2; n = 2509)	0.45
	sd	4.7 (4.6 - 4.9)	5.1 (4.9 - 5.3)	4.3 (4.1 - 4.5)	<0.001

IQR = interquartile range, n=sample size, (95% CI); sd= standard deviation; -- not calculated because sample size <10; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Hospitalizations and Deaths over time

The time series of hospitalizations (Figures S18 and S19) and person-weeks in hospital (Figures S20 and S21) give an indication of the demands on health care associated with EVD in the affected countries. This level of hospitalization has only been possible with the use of facilities built for this epidemic.

The time series of deaths (Figures S22 and S23) give insight into the human cost of the epidemic over time. Furthermore, it shows the magnitude of the need for safe burials over time. The spatial distribution of the deaths, closely follow the spatial distribution of EVD incidence (Figures S3-9).

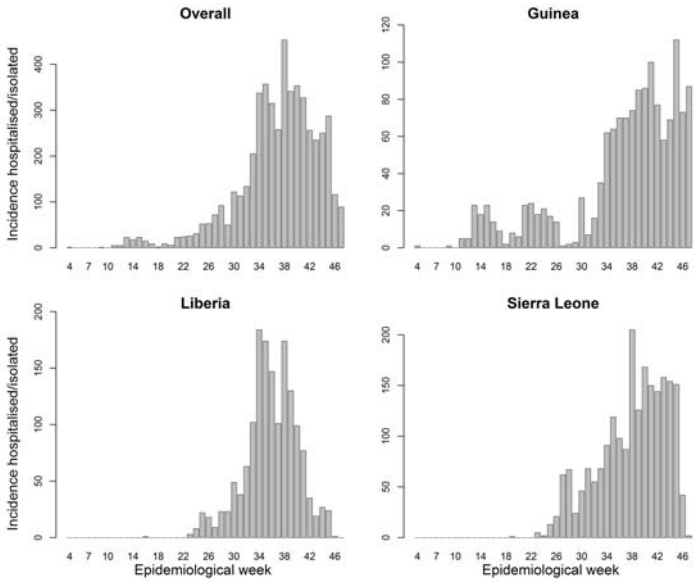

Figure S18: Incidence of confirmed and probable EVD cases hospitalized or isolated by week (based on VHF databases)

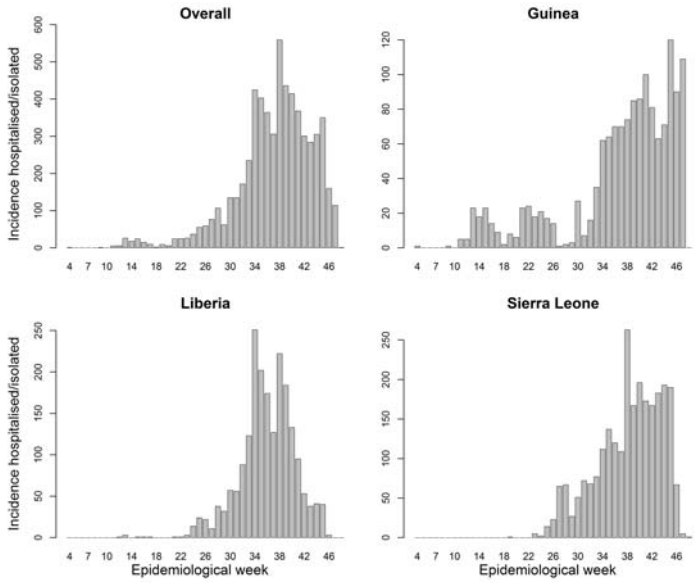

Figure S19: As Figure S18, for confirmed, probable and suspected EVD cases (based on VHF databases)

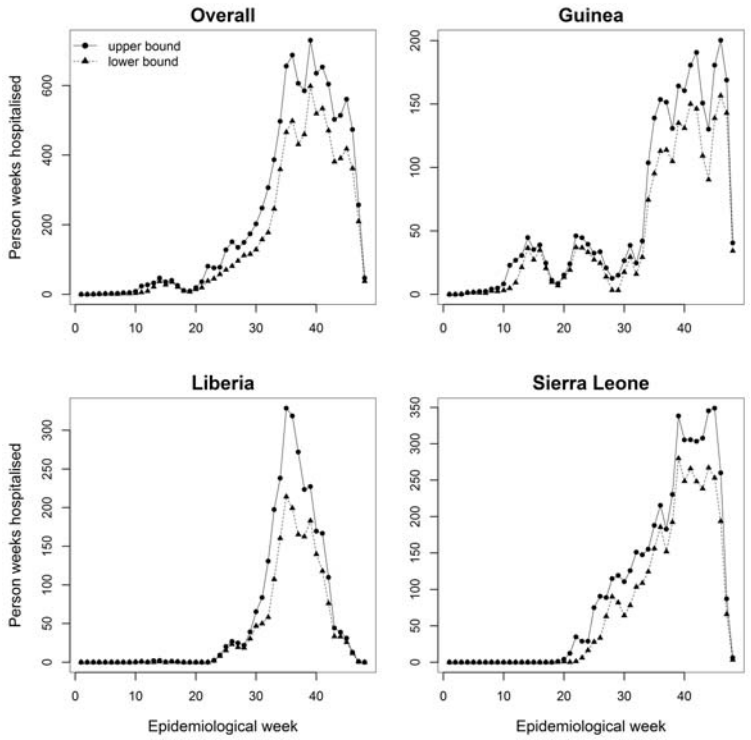

Figure S20: Number of person weeks hospitalized overall and by country among confirmed and probable EVD cases (based on VHF databases)

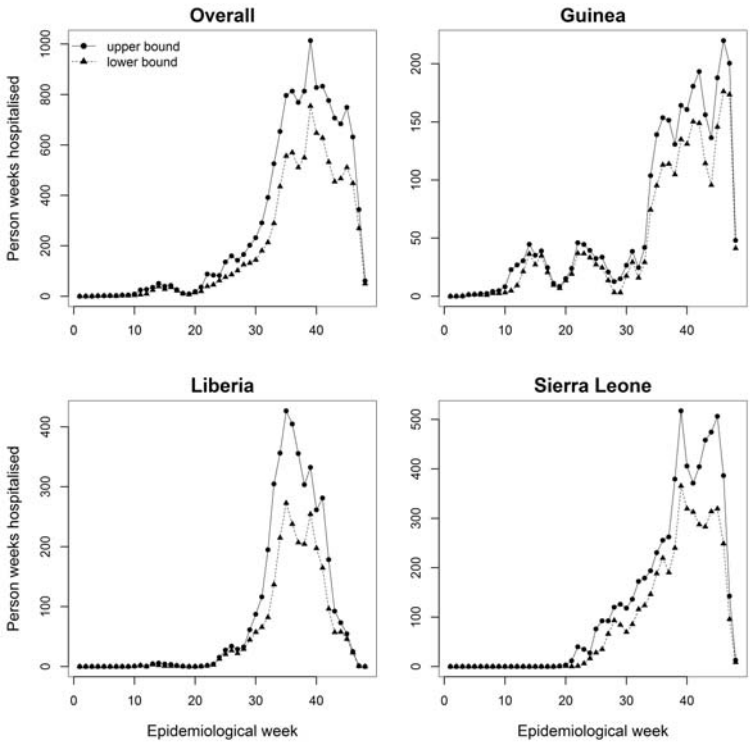

Figure S21: As Figure S20 for confirmed, probable and suspected EVD cases (based on VHF databases)

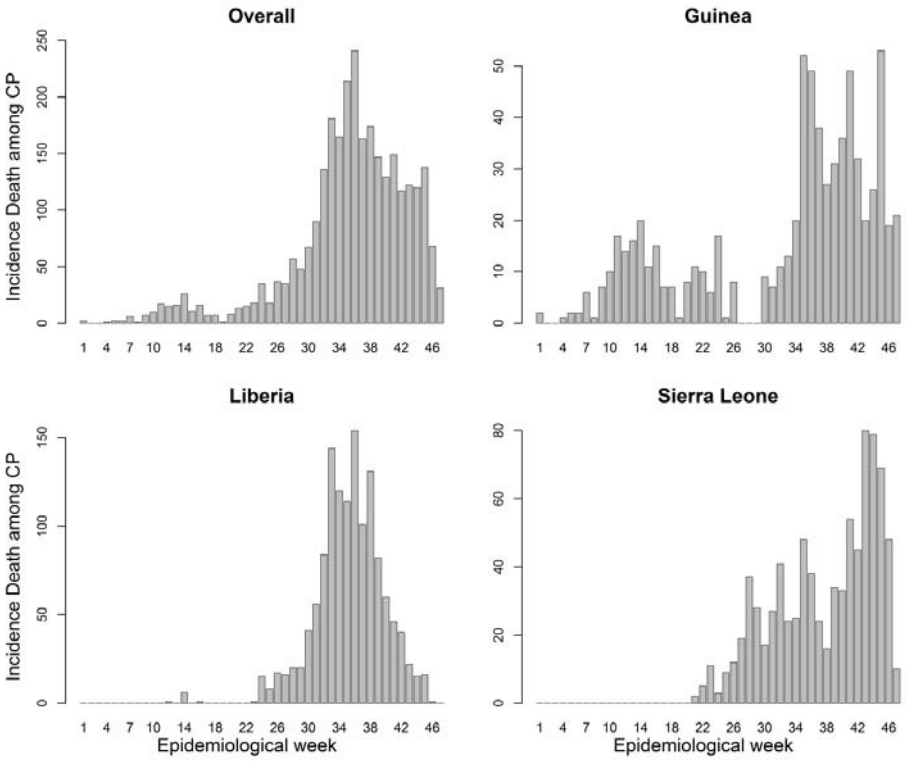

Figure S22: Deaths among confirmed and probable EVD cases reported by week overall and by country (based on VHF databases)

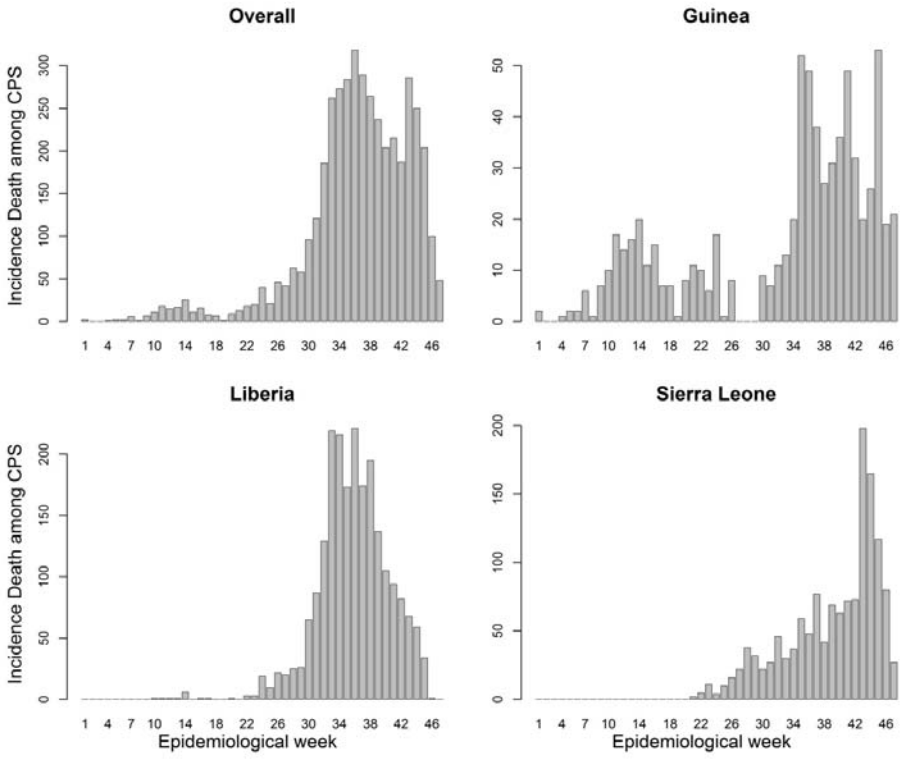

Figure S23: As Figure S22, for confirmed, probable and suspected EVD cases (based on VHF databases)

Case Fatality Rate (CFR)

We see no indication of a drop in the case fatality rate (CFR), based on definitive outcome, over time (Tables S9-S12). In fact, we see an apparent increase in CFR overall (p=0.013) from 67.8% to 76.5% among confirmed and probable EVD cases, driven by the CFR in non-HCW cases (67.8% to 77.1%, p=0.01). The late stage CFR (1 October to 25 November 2014) may be an overestimate as there are likely to be more discharges than deaths yet to be recorded for cases onset in this time period due to the mean time from hospitalization to death being shorter than the mean time from hospitalization to discharge (Table S5-S8).

CFR among Confirmed and Probable EVD Cases with definitive outcome

Table S9: Case Fatality Rate of confirmed and probable EVD cases from Guinea, Liberia and Sierra Leone (based on VHF databases)

Overall* (estimate [95% CI])

	Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
All cases, based on current status	37.8 (36.9 - 38.7)	43.5 (42.3 - 44.7)	32.3 (30.8 - 33.9)	<0.001
All cases, based on definitive outcome	70.4 (69.2 - 71.6)	67.8 (66.4 - 69.2)	76.5 (74.2 - 78.7)	0.013
Ever Hospitalized				
Hospitalized	60.7 (59.2 - 62.3)	60.0 (58.3 - 61.7)	63.7 (60.2 - 67.1)	0.39
Not hospitalized	88.4 (86.3 - 90.3)	87.3 (84.5 - 89.6)	90.8 (87.3 - 93.4)	0.72
Unknown	94.8 (93 - 96.2)	92.9 (90.2 - 94.9)	97.2 (94.1 - 98.7)	0.74
Gender				
Male	71.6 (69.9 - 73.2)	69.4 (67.4 - 71.4)	76.6 (73.2 - 79.7)	0.16
Female	68.9 (67.1 - 70.6)	66.0 (63.9 - 68.0)	75.7 (72.3 - 78.8)	0.05
Age Group				
<15 yr	68.7 (65.6 - 71.6)	64.5 (60.8 - 68.1)	75.9 (70.2 - 80.8)	0.18
15-44 yr	66.7 (65.0 - 68.3)	64.3 (62.4 - 66.2)	72.7 (69.3 - 75.9)	0.07
≥45 yr	79.4 (77.1 - 81.5)	77.5 (74.7 - 80.0)	83.2 (79.0 - 86.8)	0.47
HCW vs Non HCW				
HCW	66.8 (61.9 - 71.3)	67.3 (62.1 - 72.1)	61.5 (48.0 - 73.5)	0.80
Non-HCW	70.6 (69.4 - 71.9)	67.8 (66.3 - 69.3)	77.1 (74.7 - 79.3)	0.01

* Based on confirmed and probable EVD case with definitive outcome reported as of 25 November 2014; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Table S10: Case Fatality Rate of confirmed and probable EVD Cases from Guinea (based on VHF databases)

Guinea (estimate [95% CI])

	Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
All cases, based on current status	55.8 (53.5 - 58.1)	57.7 (54.6 - 60.7)	53.2 (49.6 - 56.8)	0.34
All cases, based on definitive outcome	65.9 (63.5 - 68.3)	63.4 (60.2 - 66.4)	70.2 (66.2 - 73.9)	0.25
Ever Hospitalized				
Hospitalized	59.3 (56.5 - 62.0)	57.7 (54.2 - 61.1)	62.2 (57.6 - 66.6)	0.47
Not hospitalized	100 (92.0 - 100)	100 (91.8 - 100)	--	1
Unknown	100 (98.1 - 100)	100 (95.4 - 100)	100 (96.8 - 100)	1
Gender				
Male	64.9 (61.3 - 68.3)	61.5 (56.8 - 66.0)	69.9 (64.4 - 74.9)	0.32
Female	66.6 (63.1 - 69.9)	65.1 (60.7 - 69.2)	69.6 (63.6 - 74.9)	0.63
Age Group				
<15 yr	71.0 (64.7 - 76.5)	73.3 (65.3 - 80.1)	67.4 (57.1 - 76.3)	0.77
15-44 yr	60.4 (57.1 - 63.7)	57.2 (53.1 - 61.3)	66.1 (60.7 - 71.2)	0.23
≥45 yr	74.4 (69.7 - 78.6)	71.4 (65.2 - 76.9)	79.0 (71.6 - 84.9)	0.59
HCW vs Non HCW				
HCW	51.6 (41.6 - 61.5)	48.6 (37.4 - 59.9)	61.9 (40.9 - 79.2)	0.70
Non-HCW	66.9 (64.4 - 69.4)	64.6 (61.3 - 67.8)	70.5 (66.5 - 74.2)	0.34

* Based on confirmed and probable EVD case with definitive outcome reported as of 25 November 2014; -- not calculated because sample size <10; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Table S11: Case Fatality Rate of confirmed and probable EVD Cases from Liberia (based on VHF databases)

Liberia (estimate [95% CI])

	Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
All cases, based on current status	38.0 (36.6 - 39.5)	46.0 (44.2 - 47.7)	24.4 (21.2 - 28.0)	<0.001
All cases, based on definitive outcome	70.6 (68.7 - 72.5)	70.4 (68.3 - 72.4)	73.2 (66.6 - 78.9)	0.78
Ever Hospitalized				
Hospitalized	62.3 (59.7 - 64.7)	61.9 (59.3 - 64.5)	69.1 (59.3 - 77.4)	0.56
Not hospitalized	83.8 (80.2 - 86.9)	85.4 (81.5 - 88.5)	76.2 (65.9 - 84.2)	0.61
Unknown	91.1 (87.2 - 93.9)	91.7 (87.6 - 94.5)	82.4 (59.0 - 93.8)	0.92
Gender				
Male	72.4 (69.7 - 75.0)	72.4 (69.6 - 75.1)	73.1 (63.3 - 81.1)	1
Female	68.6 (65.7 - 71.4)	68.1 (65.0 - 71.0)	72.7 (63.2 - 80.5)	0.75
Age Group				
<15 yr	63.2 (57.9 - 68.3)	62.6 (56.9 - 67.9)	68.6 (52.0 - 81.4)	0.85
15-44 yr	69.0 (66.4 - 71.5)	68.6 (65.8 - 71.2)	71.4 (62.5 - 79.0)	0.85
≥45 yr	79.9 (76.1 - 83.2)	80.0 (76.1 - 83.5)	79.5 (65.5 - 88.8)	1
HCW vs Non HCW				
HCW	73.7 (66.3 - 80.0)	74.5 (66.9 - 80.8)	--	0.83
Non-HCW	70.4 (68.4 - 72.3)	70.0 (67.9 - 72.1)	73.9 (67.2 - 79.7)	0.69

* Based on confirmed and probable EVD case with definitive outcome reported as of 25 November 2014; -- not calculated because sample size <10; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Table S12: Case Fatality Rate of confirmed and probable EVD Cases from Sierra Leone (based on VHF databases)

Sierra Leone (estimate [95% CI])				
	Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**	**p value**
All cases, based on current status	31.8 (30.6 - 33.1)	35.0 (33.1 - 36.8)	27.1 (25.2 - 29.1)	<0.001
All cases, based on definitive outcome	73.4 (71.4 - 75.3)	66.9 (64.3 - 69.4)	83.6 (80.4 - 86.4)	0.003
Ever Hospitalized				
Hospitalized	60.3 (57.5 - 63.1)	59.4 (56.3 - 62.5)	64.2 (57.7 - 70.3)	0.56
Not hospitalized	91.9 (89.2 - 94.0)	88.3 (83.2 - 92.0)	94.9 (91.7 - 97.0)	0.63
Unknown	95.0 (91.9 - 96.9)	90.7 (84.1 - 94.7)	96.5 (90.1 - 98.8)	0.84
Gender				
Male	75.6 (72.8 - 78.1)	70.0 (66.4 - 73.4)	85.2 (80.4 - 89.0)	0.080
Female	70.9 (67.9 - 73.7)	63.4 (59.5 - 67.1)	81.7 (77.0 - 85.6)	0.021
Age Group				
<15 yr	72.2 (67.4 - 76.5)	61.7 (55.0 - 67.9)	84.0 (76.6 - 89.4)	0.088
15-44 yr	68.8 (65.9 - 71.5)	63.0 (59.4 - 66.4)	80.4 (75.4 - 84.6)	0.025
≥45 yr	82.7 (79.0 - 85.8)	78.3 (73.1 - 82.7)	87.9 (82.0 - 92.0)	0.47
HCW vs Non HCW				
HCW	69.1 (61.0 - 76.1)	69.6 (60.6 - 77.4)	64.0 (44.5 - 79.8)	0.95
Non-HCW	73.7 (71.7 - 75.7)	66.6 (63.9 - 69.3)	84.5 (81.3 - 87.3)	0.0026

*Based on confirmed and probable EVD case with definitive outcome reported as of 25 November 2014; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

CFR among Confirmed, Probable and Suspected EVD Cases with definitive outcome

Table S13: Case Fatality Rate of confirmed, probable and suspected EVD cases from overall (based on VHF databases)

Overall* (estimate [95% CI])				
	Dec 2013-25 Nov 2014	**Dec 2013-30 Sept 2014**	**1 Oct-25 Nov 2014**	**p value**
All cases, based on current status	38.1 (37.4 - 38.9)	44.2 (43.2 - 45.3)	33.4 (32.1 - 34.7)	<0.001
All cases, based on definitive outcome	74.5 (73.5 - 75.5)	71.8 (70.6 - 73.0)	80.8 (79.0 - 82.4)	0.0032
Ever Hospitalized				
Hospitalized	61.9 (60.5 - 63.3)	61.2 (59.6 - 62.8)	64.6 (61.4 - 67.6)	0.39
Not hospitalized	90.0 (88.6 - 91.3)	88.3 (86.2 – 90.0)	93.1 (90.9 - 94.7)	0.47
Unknown	96.5 (95.3 - 97.4)	95.6 (93.9 - 96.8)	98.1 (96.0 - 99.1)	0.81
Gender				
Male	75.5 (74.2 - 76.9)	73.4 (71.7 – 75.0)	80.5 (77.9 - 82.9)	0.10
Female	73.1 (71.7 - 74.6)	69.9 (68.1 - 71.7)	80.4 (77.8 - 82.8)	0.016
Age Group				
<15 yr	73.1 (70.5 - 75.5)	67.7 (64.4 - 70.9)	82.2 (78.0 - 85.7)	0.046
15-44 yr	70.1 (68.7 - 71.5)	68.0 (66.3 - 69.6)	75.6 (72.8 - 78.2)	0.064
≥45 yr	83.1 (81.4 - 84.8)	80.9 (78.7 – 83.0)	87.5 (84.5 – 90.0)	0.33
HCW vs Non HCW				
HCW	69.7 (65.4 - 73.7)	69.4 (64.6 - 73.8)	70.3 (59.1 - 79.5)	1
Non-HCW	74.8 (73.8 - 75.8)	72.0 (70.7 - 73.2)	81.2 (79.3 - 82.9)	0.003

* Based on confirmed, probable and suspected EVD case with definitive outcome reported as of 25 November 2014; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Table S14: Case Fatality Rate of confirmed, probable and suspected EVD Cases from Guinea (based on VHF databases)

Guinea (estimate [95% CI])

	Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
All cases, based on current status	53.9 (51.6 - 56.2)	57.7 (54.6 - 60.7)	49.1 (45.6 - 52.6)	0.051
All cases, based on definitive outcome	65.8 (63.4 - 68.2)	63.4 (60.2 - 66.4)	69.9 (66.0 - 73.6)	0.27
Ever Hospitalized				
Hospitalized	59.2 (56.4 - 61.9)	57.7 (54.2 - 61.1)	61.9 (57.3 - 66.4)	0.49
Not hospitalized	100 (92.0 - 100)	100 (91.8 - 100)	--	--
Unknown	100 (98.1 - 100)	100 (95.4 - 100)	100 (96.8 - 100)	1
Gender				
Male	64.8 (61.2 - 68.2)	61.5 (56.8 – 66.0)	69.7 (64.1 - 74.7)	0.33
Female	66.5 (63.0 - 69.9)	65.1 (60.7 - 69.2)	69.3 (63.4 - 74.6)	0.65
Age Group				
<15 yr	70.7 (64.4 - 76.2)	73.3 (65.3 - 80.1)	66.7 (56.4 - 75.5)	0.73
15-44 yr	60.4 (57.1 - 63.6)	57.2 (53.1 - 61.3)	65.9 (60.4 – 71.0)	0.24
≥45 yr	74.4 (69.7 - 78.6)	71.4 (65.2 - 76.9)	79.0 (71.6 - 84.9)	0.59
HCW vs Non HCW				
HCW	51.6 (41.6 - 61.5)	48.6 (37.4 - 59.9)	61.9 (40.9 - 79.2)	0.70
Non-HCW	66.8 (64.3 - 69.3)	64.6 (61.3 - 67.8)	70.2 (66.2 – 74.0)	0.36

*Based on confirmed, probable and suspected EVD case with definitive outcome reported as of 25 November 2014; -- not calculated because sample size <10; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Table S15: Case Fatality Rate of confirmed, probable and suspected EVD Cases from Liberia (based on VHF databases)

Liberia (estimate [95% CI])

	Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
All cases, based on current status	39.3 (38.1 - 40.5)	47.0 (45.6 - 48.4)	31.7 (29.0 - 34.4)	<0.001
All cases, based on definitive outcome	74.9 (73.4 - 76.3)	73.9 (72.2 - 75.5)	81.4 (77.4 - 84.9)	0.23
Ever Hospitalized				
Hospitalized	63.7 (61.5 - 65.9)	63.3 (61.0 - 65.6)	68.9 (61.5 - 75.4)	0.55
Not hospitalized	86.7 (84.4 - 88.7)	86.1 (83.4 - 88.4)	88.9 (83.9 - 92.5)	0.82
Unknown	94.6 (92.2 - 96.3)	94.7 (92.2 - 96.5)	93.5 (82.5 - 97.8)	1
Gender				
Male	76.5 (74.4 - 78.4)	75.8 (73.6 - 77.9)	81.0 (75.3 - 85.6)	0.58
Female	73.0 (70.7 - 75.2)	71.6 (69.1 - 74.0)	81.6 (75.6 - 86.4)	0.28
Age Group				
<15 yr	67.8 (63.3 - 71.9)	65.1 (60.2 - 69.7)	82.4 (71.6 - 89.6)	0.28
15-44 yr	72.4 (70.3 - 74.4)	71.6 (69.4 - 73.7)	77.0 (70.9 - 82.1)	0.55
≥45 yr	83.5 (80.8 - 85.9)	82.8 (79.7 - 85.5)	87.3 (80.4 – 92.0)	0.76
HCW vs Non HCW				
HCW	76.6 (70.3 - 81.9)	76.3 (69.7 - 81.9)	78.6 (52.4 - 92.4)	1
Non-HCW	74.8 (73.2 - 76.3)	73.7 (72.0 - 75.3)	81.5 (77.5 - 85.0)	0.22

* Based on confirmed, probable and suspected EVD case with definitive outcome reported as of 25 November 2014; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Table S16: Case Fatality Rate of confirmed, probable and suspected EVD Cases from Sierra Leone (based on VHF databases)

Sierra Leone (estimate [95% CI])

	Dec 2013-25 Nov 2014	Dec 2013-30 Sept 2014	1 Oct-25 Nov 2014	p value
All cases, based on current status	33.3 (32.2 - 34.4)	36.6 (35.1 - 38.2)	30.0 (28.5 - 31.7)	<0.001
All cases, based on definitive outcome	78.6 (77.0 - 80.1)	72.8 (70.6 - 74.9)	86.5 (84.2 - 88.5)	0.004
Ever Hospitalized				
Hospitalized	61.9 (59.3 - 64.4)	60.6 (57.6 - 63.5)	66.1 (60.6 - 71.1)	0.44
Not hospitalized	93.2 (91.3 - 94.7)	91.3 (87.9 - 93.8)	94.8 (92.5 - 96.5)	0.74
Unknown	97.0 (95.2 - 98.1)	95.6 (92.4 - 97.5)	98.0 (94.9 - 99.2)	0.91
Gender				
Male	80.0 (77.8 - 82.0)	75.1 (72.1 - 77.8)	87.0 (83.7 - 89.8)	0.091
Female	76.9 (74.5 - 79.0)	70.1 (66.8 - 73.2)	85.6 (82.2 - 88.4)	0.022
Age Group				
<15 yr	78.6 (74.9 - 81.9)	68.6 (62.9 - 73.8)	88.3 (83.5 - 91.9)	0.072
15-44 yr	73.0 (70.7 - 75.3)	67.9 (64.8 - 70.8)	81.6 (77.7 - 84.9)	0.039
≥45 yr	87.1 (84.5 - 89.4)	83.2 (79.2 - 86.5)	91.6 (87.9 - 94.3)	0.42
HCW vs Non HCW				
HCW	71.5 (64.2 - 77.9)	71.0 (62.4 - 78.2)	71.8 (56.2 - 83.5)	1
Non-HCW	79.0 (77.4 - 80.6)	72.9 (70.7 - 75.1)	87.1 (84.8 - 89.1)	0.004

*Based on confirmed, probable and suspected EVD case with definitive outcome reported as of 25 November 2014; p value for chi-square test for difference in estimates from December 2013-30 September 2014 vs. 1 October-25 November 2014 time periods

Demographic Characteristics and Signs and Symptoms of EVD Cases

As presented previously[1], Tables S17 and S18 show the demographic characteristics, signs and symptoms reported between symptom onset and clinical assessment of confirmed and probable (Table S17) and confirmed, probable and suspected (Table S18) EVD cases overall and by final outcome. These analyses, as performed previously[1], were restricted to patients who had a definitive outcome by the time of analysis and excluded patients reported post-mortem.

Among confirmed and probable cases, after controlling for country, male gender and being 15-44 years old were protective against a fatal outcome, while individuals who were ≥45 years old were at an increased risk of death. General symptoms associated with risk of death include vomiting; diarrhea; pain in the muscles or chest; cough; difficulty breathing or swallowing; conjunctivitis; sore throat; confusion; hiccups; jaundice; rash; coma. All hemorrhagic symptoms measured in the standardized case report form, with the exception of blood in stool and urine and other bleeding, were significantly associated with an increased risk of death.

The same trends were observed among confirmed, probable and suspected cases, with the addition that being a health care worker was protective against a fatal outcome, and vomiting, muscle pain, conjunctivitis and coma were no longer significantly associated with risk of death. Of the hemorrhagic symptoms, the same trends were observed except hematemesis and blood in vomit were no longer significantly associated with risk of death.

These results are similar to our previous report of cases reported during the first nine months of the epidemic[1].

Among Confirmed and Probable EVD Cases

Table S17: Demographic Characteristics and Signs and Symptoms in confirmed and probable EVD Cases with a Definitive Clinical Outcome in Guinea, Liberia and Sierra Leone (based on VHF databases)*

	Confirmed, Probable and Suspected EVD Cases								
	All cases		Fatal		Recovered		OR (95% CI)[α]		
	n	Proportion	n	Proportion	n	Proportion	OR	Lower	Upper
Gender (% Male)	2830/5564	0.51	2026/3909	0.52	804/1655	0.49	0.88	0.78	0.99
Age Group									
<15 yr	920/5440	0.17	632/3814	0.17	288/1626	0.18	0.91	0.78	1.06
15-44 yr	3191/5440	0.59	2127/3814	0.59	1064/1626	0.65	0.67	0.59	0.75
≥ 45 yr	1329/5440	0.24	1055/3814	0.24	274/1626	0.17	1.90	1.64	2.20
HCW	388/5616	0.07	259/3952	0.07	129/1664	0.08	0.83	0.67	1.04
Signs and Symptoms									
General symptoms									
Fever	3440/3952	0.87	2312/2656	0.87	1128/1296	0.87	1.04	0.85	1.26
Fatigue	3098/3865	0.80	2091/2595	0.81	1007/1270	0.79	1.14	0.96	1.35
Loss of appetite	2685/3613	0.74	1810/2440	0.74	875/1173	0.75	0.98	0.83	1.15
Vomiting	2402/3657	0.66	1649/2458	0.67	753/1199	0.63	1.28	1.10	1.49
Diarrhea	2307/3624	0.64	1619/2468	0.66	688/1156	0.60	1.37	1.18	1.59
Headache	2122/3504	0.61	1411/2357	0.60	711/1147	0.62	0.94	0.82	1.09
Abdominal Pain	1764/3369	0.52	1196/2273	0.53	568/1096	0.52	1.03	0.89	1.19
Muscle Pain	1694/3378	0.50	1169/2278	0.51	525/1100	0.48	1.17	1.01	1.35
Joint Pain	1616/3253	0.50	1123/2208	0.51	493/1045	0.47	1.14	0.99	1.33
Chest Pain	1179/2815	0.42	838/1906	0.44	341/909	0.38	1.28	1.09	1.51
Cough	868/2775	0.31	626/1880	0.33	242/895	0.27	1.34	1.13	1.60
Difficulty Breathing	751/2845	0.26	593/1956	0.30	158/889	0.18	2.01	1.65	2.45
Difficulty Swallowing	721/2642	0.27	550/1816	0.30	171/826	0.21	1.66	1.37	2.03
Conjunctivitis	734/2788	0.26	520/1899	0.27	214/889	0.24	1.20	1.00	1.45
Sore Throat	546/2510	0.22	404/1709	0.24	142/801	0.18	1.42	1.15	1.76
Confused	332/2554	0.13	254/1719	0.15	78/835	0.09	1.72	1.32	2.26
Hiccups	379/3053	0.12	291/2075	0.14	88/978	0.09	1.69	1.32	2.19
Jaundice	356/2584	0.14	257/1738	0.15	99/846	0.12	1.33	1.04	1.71
Eye Pain	209/2519	0.08	144/1690	0.09	65/829	0.08	1.09	0.81	1.49
Rash	156/2591	0.06	116/1743	0.07	40/848	0.05	1.44	1.01	2.11
Coma/Unconscious	152/2535	0.06	131/1706	0.08	21/829	0.03	3.21	2.06	5.28
Hemorrhagic Symptoms									
Unexplained bleeding	373/3138	0.12	288/2133	0.14	85/1005	0.08	1.98	1.52	2.59
Hematemesis	47/2608	0.02	38/1747	0.02	9/861	0.01	2.09	1.05	4.64
Blood in Stool	85/2801	0.03	64/1872	0.03	21/929	0.02	1.60	0.98	2.70
Bleeding Gums	53/2796	0.02	45/1870	0.02	8/926	0.01	2.74	1.36	6.31
Bloody Nose	36/2791	0.01	32/1870	0.02	4/921	0.00	3.99	1.57	13.4
Bloody Cough	28/2780	0.01	24/1860	0.01	4/920	0.00	2.85	1.10	9.74
Bleeding Other	22/2608	0.01	17/1746	0.01	5/862	0.01	1.76	0.69	5.39
Bleeding at Injection Site	32/2787	0.01	29/1864	0.02	3/923	0.00	4.69	1.66	19.6
Blood in Vomit	32/2596	0.01	27/1739	0.02	5/857	0.01	2.51	1.05	7.44
Blood from vagina§	30/1380	0.02	27/896	0.03	3/484	0.01	4.27	1.50	17.9
Blood in urine	15/2776	0.005	11/1854	0.006	4/922	0.004	1.33	0.45	4.82

* Data are based on VHF databases as of 25 November 2014. Total numbers are the numbers of cases with data on the variable in question. NA denotes not applicable. † Odds ratios are adjusted for country. CI denotes confidence interval. ‡ Fever was defined as a body temperature above 38°C; however, in practice, health care workers at the district level often do not have a medical thermometer and simply ask whether the person's body temperature is more elevated than usual. § Percentages reflect only female cases.

Among Confirmed, Probable and Suspected EVD Cases

Table S18: As Table S17, for Confirmed, Probable and Suspected EVD Cases (based on VHF databases)

	Confirmed, Probable and Suspected EVD Cases								
	All cases		Fatal		Recovered		OR (95% CI)[α]		
	n	Proportion	n	Proportion	n	Proportion	OR	Lower	Upper
Gender (% Male)	3852/7456	0.52	2910/5546	0.52	942/1910	0.49	0.89	0.80	0.98
Age Group									
<15 yr	1206/7241	0.17	881/5360	0.16	325/1881	0.17	0.92	0.80	1.06
15-44 yr	4142/7241	0.57	2905/5360	0.54	1237/1881	0.66	0.62	0.56	0.7
≥ 45 yr	1893/7241	0.26	1574/5360	0.29	319/1881	0.17	2.03	1.78	2.33
HCW	459/7533	0.06	320/5611	0.06	139/1922	0.07	0.78	0.63	0.96
Signs and Symptoms									
General symptoms									
Fever	4515/5331	0.85	3204/3815	0.84	1311/1516	0.86	0.86	0.73	1.03
Fatigue	4068/5214	0.78	2895/3720	0.78	1173/1494	0.79	1.03	0.89	1.19
Loss of appetite	3576/4943	0.72	2555/3551	0.72	1021/1392	0.73	0.94	0.82	1.08
Vomiting	3076/4962	0.62	2211/3543	0.62	865/1419	0.61	1.14	1.00	1.29
Diarrhea	2917/4903	0.59	2121/3526	0.60	796/1377	0.58	1.17	1.03	1.33
Headache	2802/4804	0.58	1976/3436	0.58	826/1368	0.60	0.93	0.82	1.06
Abdominal Pain	2407/4641	0.52	1723/3329	0.52	684/1312	0.52	0.98	0.86	1.12
Muscle Pain	2263/4662	0.49	1633/3345	0.49	630/1317	0.48	1.06	0.93	1.20
Joint Pain	2177/4520	0.48	1584/3261	0.49	593/1259	0.47	1.05	0.92	1.20
Chest Pain	1638/4020	0.41	1220/2897	0.42	418/1123	0.37	1.21	1.05	1.39
Cough	1195/3956	0.30	889/2850	0.31	306/1106	0.28	1.19	1.02	1.39
Difficulty Breathing	1160/4092	0.28	950/2988	0.32	210/1104	0.19	1.98	1.67	2.35
Difficulty Swallowing	1009/3850	0.26	800/2811	0.28	209/1039	0.20	1.58	1.33	1.88
Conjunctivitis	936/3976	0.24	681/2876	0.24	255/1100	0.23	1.05	0.89	1.24
Sore Throat	741/3658	0.20	568/2646	0.21	173/1012	0.17	1.31	1.09	1.58
Confused	495/3580	0.14	402/2543	0.16	93/1037	0.09	2.01	1.59	2.57
Hiccups	515/4222	0.12	411/3036	0.14	104/1186	0.09	1.69	1.35	2.14
Jaundice	510/3625	0.14	384/2571	0.15	126/1054	0.12	1.33	1.07	1.65
Eye Pain	270/3516	0.08	191/2487	0.08	79/1029	0.08	1.00	0.77	1.33
Rash	208/3625	0.06	161/2571	0.06	47/1054	0.04	1.44	1.04	2.04
Coma/Unconscious	226/3542	0.06	201/2514	0.08	25/1028	0.02	3.54	2.36	5.53
Hemorrhagic Symptoms									
Unexplained bleeding	480/4302	0.11	380/3094	0.12	100/1208	0.08	1.86	1.47	2.38
Hematemesis	69/3619	0.02	56/2567	0.02	13/1052	0.01	1.76	0.99	3.38
Blood in Stool	100/3813	0.03	77/2692	0.03	23/1121	0.02	1.51	0.95	2.47
Bleeding Gums	73/3807	0.02	63/2689	0.02	10/1118	0.01	2.60	1.39	5.41
Bloody Nose	51/3801	0.01	46/2687	0.02	5/1114	0.00	3.87	1.68	11.2
Bloody Cough	36/3786	0.01	32/2674	0.01	4/1112	0.00	3.22	1.27	10.9
Bleeding Other	31/3616	0.01	25/2562	0.01	6/1054	0.01	1.80	0.78	4.87
Bleeding at Injection Site	40/3796	0.01	36/2681	0.01	4/1115	0.00	3.66	1.46	12.3
Blood in Vomit	43/3603	0.01	36/2554	0.01	7/1049	0.01	1.95	0.92	4.81
Blood from vagina§	45/1839	0.02	38/1269	0.03	7/570	0.01	2.16	1.02	5.31
Blood in urine	20/3777	0.01	14/2663	0.01	6/1114	0.01	0.93	0.37	2.65

* Data are based on VHF databases as of 25 November 2014. Total numbers are the numbers of cases with data on the variable in question. NA denotes not applicable. † Odds ratios are adjusted for country. CI denotes confidence interval. ‡ Fever was defined as a body temperature above 38°C; however, in practice, health care workers at the district level often do not have a medical thermometer and simply ask whether the person's body temperature is more elevated than usual. § Percentages reflect only female cases.

Estimation of *R* and Forward Projections

We estimated the recent reproduction number (R_t) and doubling time by country using the same methods as previously[1]. Estimates of R_t based on confirmed and probable EVD cases (Table S19) suggest that incidence is no longer increasing in each of the three countries (R_t not significantly different from 1). Analysis of the incidence of confirmed, probable and suspected EVD cases (Table S20) indicates a slow increase in incidence (R_t>1) in Guinea, a decrease in Liberia (R_t<1) and plateauing in Sierra Leone (R_t not significantly different from 1).

Figure S24 presents the smoothed trends in the estimated reproduction number over time. In Guinea, the epidemic has been stable since mid-September (incidence fluctuating within bounds). In Liberia, the reproduction number has declined since early August (R_t<1), although with a recent upward trend associated with a plateauing in incidence levels. In Sierra Leone, the reproduction number has been relatively stable from mid-July until October at a value >1, after which it dropped to very close to 1. Further control efforts are needed to in all three countries to push the reproduction number substantially below one and thus to eliminate infection from the human population.

Figures S25-26 present our current projections of the weekly number of new cases per country (in colours), based on our parametrically estimated serial interval distribution, overlaid to our initial projections[1] (in grey). These plots highlight that much has been achieved in all three countries to reduce transmission and slow epidemic growth, but that zero infection is still a distant goal.

Estimation of R and Doubling Time

Table S19: Estimated reproduction numbers (R_t) and doubling times (with 95% credible intervals (CrI)), based on dates of onset of confirmed and probable EVD cases (based on the supplemented daily incidence time series as described in Data Sources)

		Serial interval = 11	Serial interval = 13	Serial interval = 14.2 *
R_t (95% CrI)	Guinea	1.00 (0.92 ; 1.09)	0.98 (0.9 ; 1.09)	0.99 (0.90 ; 1.08)
	Liberia	0.93 (0.86 ; 1.02)	0.93 (0.86 ; 1.01)	0.93 (0.85 ; 1.02)
	Sierra Leone	0.99 (0.95 ; 1.03)	1.00 (0.95 ; 1.05)	0.99 (0.95 ; 1.03)
Doubling time (95% CrI)	Guinea	8455.5 (-92.25 | 90.27)**	-576.52 (-86.98 | 107.35)**	-718.16 (-93.14 | 133.54)**
	Liberia	-109.34 (-52.28 | 460.81)**	-124.56 (-59.7 | 832.82)**	-132.03 (-60.32 | 732.06)**
	Sierra Leone	-985.47 (-168.11 | 239.96)**	-3322.71 (-178.2 | 206.64)**	-723.07 (-170 | 418.62)**

Notes: based on dates of onset of confirmed and probable EVD cases from 20 October 2014 to 7 December 2014 for Guinea and from 13 October 2014 to 30 November 2014 for Liberia and Sierra Leone. *Mean of the parametrically estimated serial interval distribution (Table 4). Negative doubling times correspond to declining incidence. Results marked as ** are exclusion intervals, reflecting uncertainty as to whether incidence is increasing or decreasing. Note that in this case, the 95% credibility region is [- infinity; lower bound] | [upper bound;+infinity]; i.e. 0 is not in the 95% range since an infinite doubling time represents constant incidence over time.

Table S20: As Table S19, for confirmed, probable and suspected EVD cases (based on the supplemented daily incidence time series as described in Data Sources)

		Serial interval = 11	Serial interval = 13	Serial interval = 14.1 *
R_t (95% CrI)	Guinea	1.10 (1.02 ; 1.19)	1.11 (1.02 ; 1.20)	1.13 (1.04 ; 1.22)
	Liberia	0.89 (0.84 ; 0.94)	0.88 (0.84 ; 0.93)	0.88 (0.83 ; 0.93)
	Sierra Leone	1.00 (0.95 ; 1.03)	0.99 (0.96 ; 1.02)	0.99 (0.95 ; 1.02)
Doubling time (95% CrI)	Guinea	79.00 (43.34 ; 420.26)	84.35 (48.03 ; 406.03)	80.37 (46.47 ; 277.77)
	Liberia	-68.66 (-137.78 ; -45.68)	-70.79 (-122.28 ; -52.15)	-74.60 (-133.06 ; -51.46)
	Sierra Leone	-1253.68 (-166.62 | 300.95)**	-630.75 (-199.61 | 430.19)**	-607.41 (-183.71 | 550.65)**

Notes: based on dates of onset of confirmed, probable and suspected EVD cases from 20 October 2014 to 7 December 2014 for Guinea and from 13 October 2014 to 30 November 2014 for Liberia and Sierra Leone. *Mean of the parametrically estimated serial interval distribution (Table 4). Negative doubling times correspond to declining incidence. Results marked as ** are exclusion intervals, reflecting uncertainty as to whether incidence is increasing or decreasing. Note that in this case, the 95% credibility region is [- infinity; lower bound] | [upper bound;+infinity]; i.e. 0 is not in the 95% range since an infinite doubling time represents constant incidence over time.

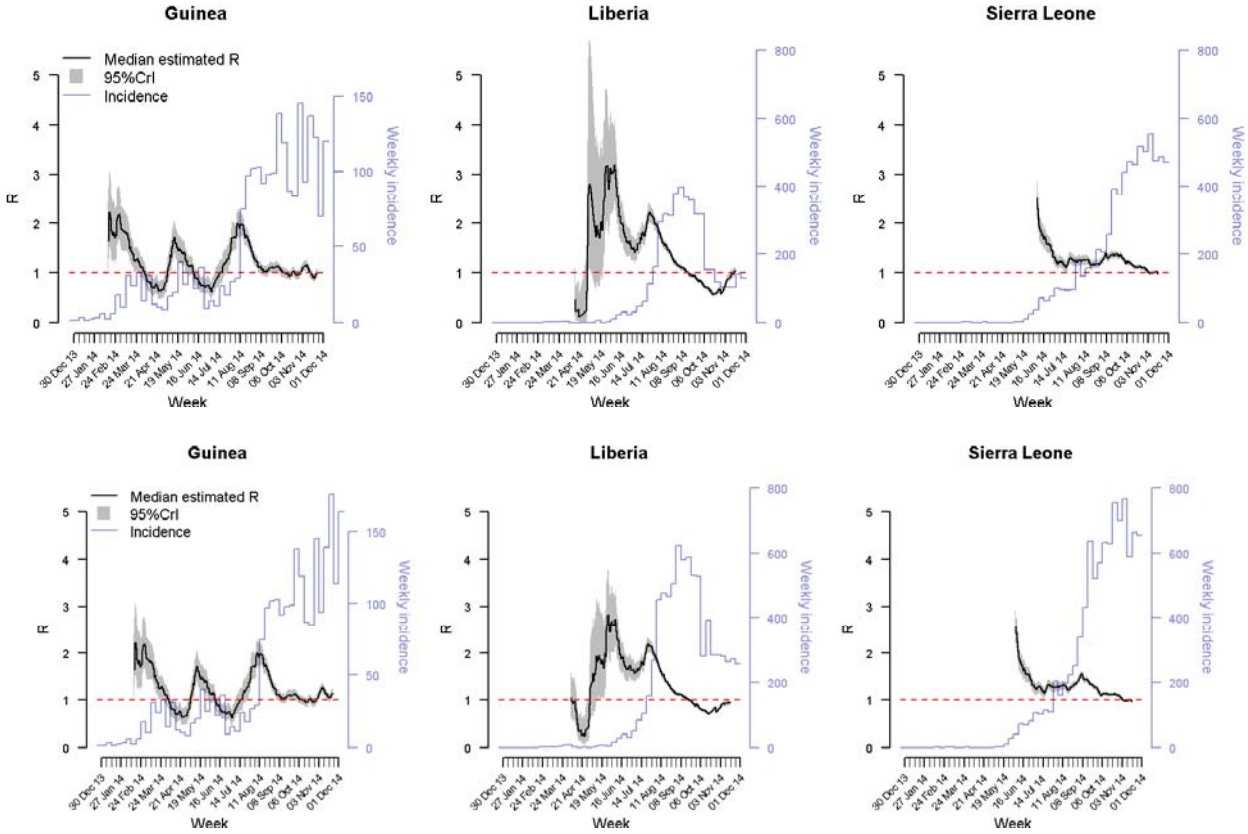

Figure S24: Estimation of R_t over time for Guinea, Liberia and Sierra Leone based on confirmed and probable EVD cases (upper panel) and separately for confirmed, probable and suspected EVD cases (lower panel) (based on the supplemented daily incidence time series as described in Data Sources). R_t is estimated over sliding 4-week windows and plotted at the midpoint of these windows.

Forward Projections

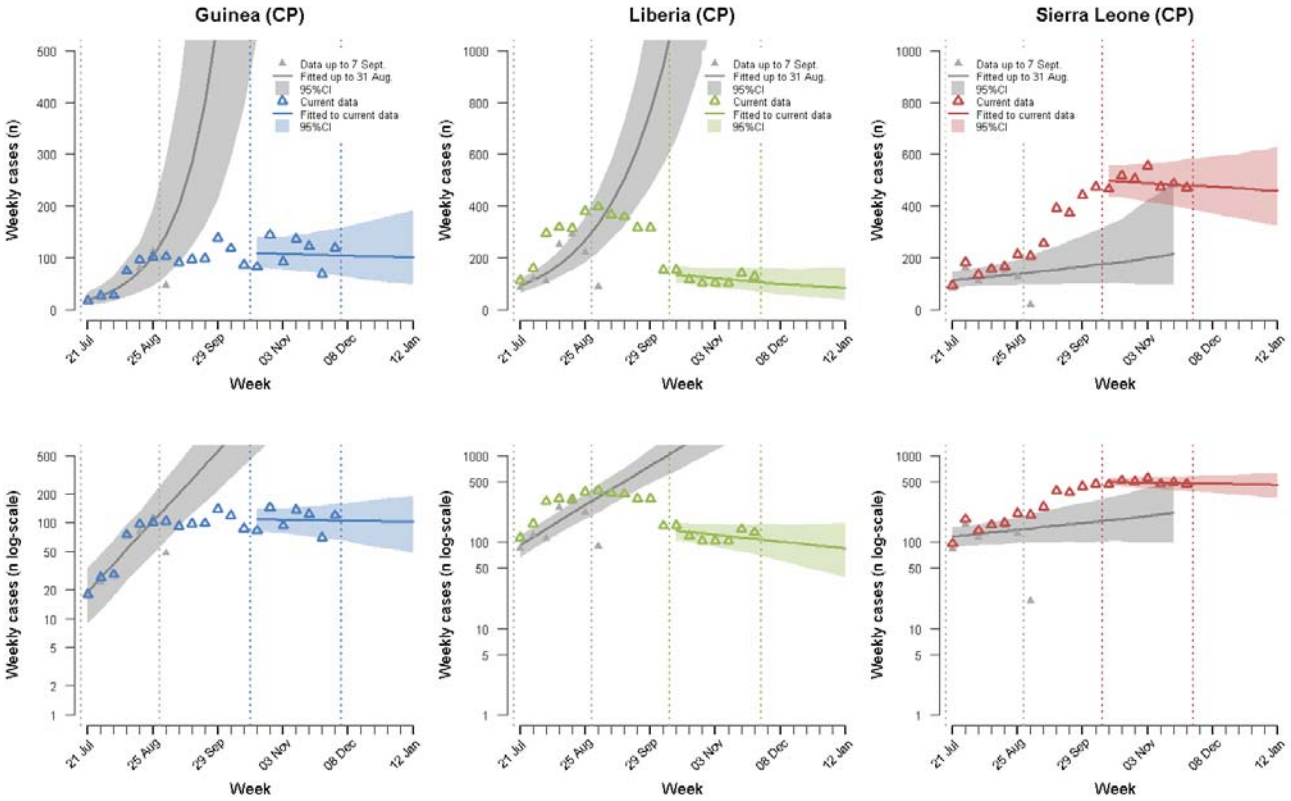

Figure S25: Observed and projected confirmed and probable case incidence by week of symptom onset (based on the supplemented daily incidence time series as described in Data Sources). Observed and projected weekly case incidence in Guinea, Liberia, and Sierra Leone are shown on linear (upper panels) and logarithmic (lower panels) scales. Black/grey shading shows projections published in September[1]. Current estimates for all three countries are based on cases onset from 20 October 2014 to 7 December 2014 for Guinea and from 13 October 2014 to 30 November 2014 for Liberia and Sierra Leone. Those date ranges are delineated by the colored vertical dotted lines. Grey points and curves show the data and projections presented in our previous paper[1] with estimates based on the period from 21 July 2014 to 31 August 2014.

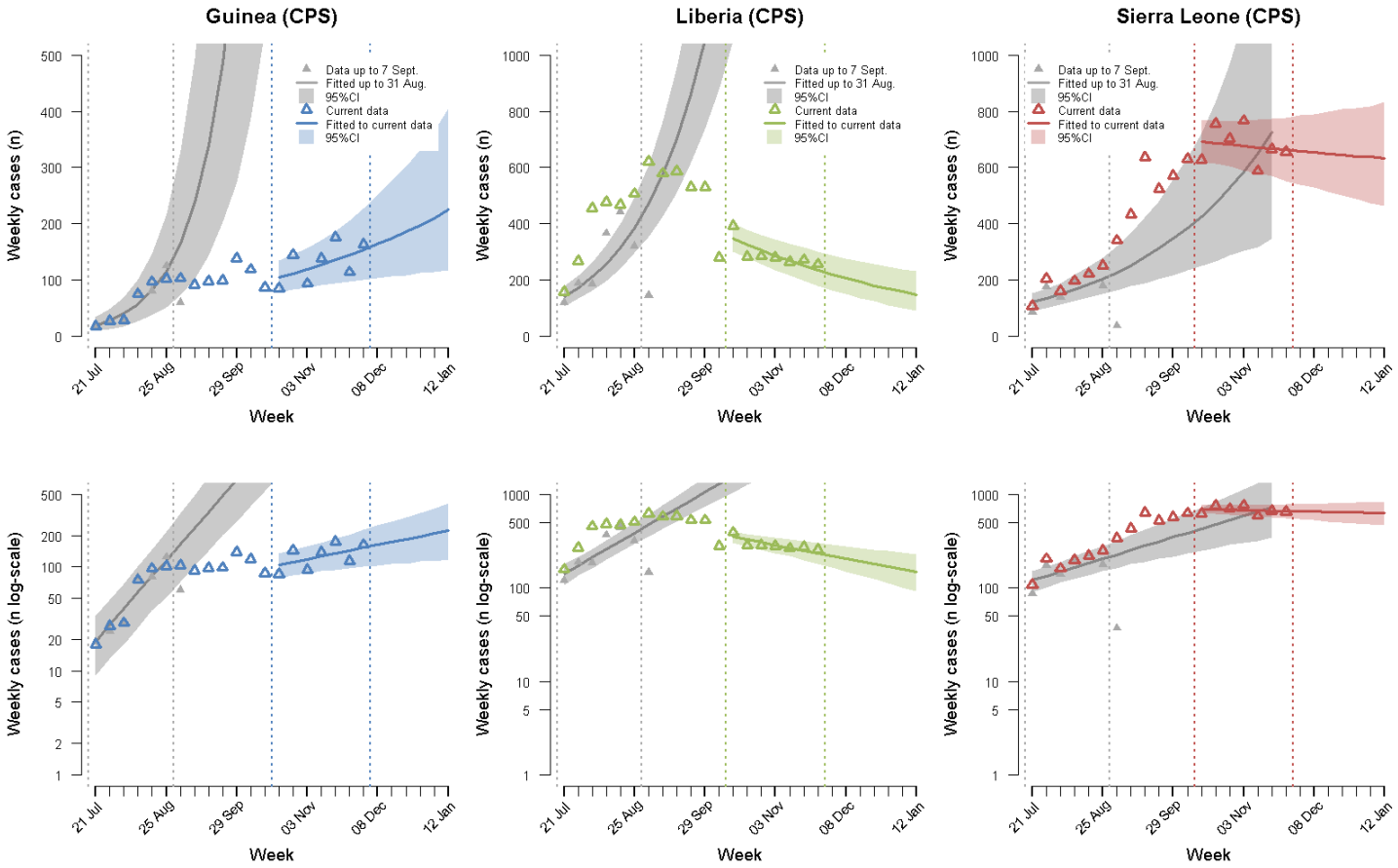

Figure S26: As Figure S25, for confirmed, probable and suspected EVD cases (based on the supplemented daily incidence time series as described in Data Sources).

References

1. WHO Ebola Response Team. Ebola virus disease in West Africa--the first 9 months of the epidemic and forward projections. N Engl J Med 2014;371:1481-95. doi: 10.056/NEJMoa1411100. Epub 2014 Sep 23.

2. World Health Organization. Case definition recommendations for Ebola or Marburg Virus Diseases, as of 09 August 2014. Available at: http://www.who.int/csr/resources/publications/ebola/ebola-case-definition-contact-en.pdf. Last accessed 19/12/2012. 2014.