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Emerging Problems in Infectious Diseases

Descriptive analyses and risk of death due to Ebola Virus Disease, West Africa, 2014

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Abstract

Introduction: Since the first case of Ebola virus disease (EVD) in Guinea in 2013, major outbreaks have been reported in West Africa.
Methodology: Cases and fatalities of EVD caused by Zaire Ebola virus (ZEBOV) were evaluated, and the risks of dying in the general population and in healthcare workers were assessed.
Results: The case fatality rate estimated for EVD was 76.4% in 20 studies. Cumulative proportion of fatal cases in West Africa was 42.9%, 30.1%, and 64.2% in Liberia, Sierra Leone, and Guinea, respectively. The proportion of total deaths in Liberia, Sierra Leone, and Guinea was 42.5%, 35.8%, and 21.6%, respectively. Healthcare workers were at higher risk of dying compared with the general public, and the same applied to intense transmission countries and to countries with sufficient bed capacities. The declaration of a health emergency "out-of-control" situation by the World Health Organization on 8 August 2014 reduced the risk of death among patients. Factors including deplorable healthcare delivery infrastructure in war-ravaged regions of Africa, the impotence of governments to enforce public health regulations, and the loss of confidence in public healthcare delivery programs were key among others factors that enhanced the spread and magnitude of outbreaks.
Conclusions: The findings underscore the need for an overall re-appraisal of the healthcare systems in African countries and the ability to cope with widespread epidemic challenges. Outbreaks like that of Ebola diseases should be handled not just as a medical emergency but also a socio-economic problem with significant negative economic impacts.

Key words: Ebola; West Africa; case fatality rate; filovirus.

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Introduction

In November 1994, the case of a lone Taï Ebola virus disease (EVD) occurred in a Swiss female ethologist in Cote d'Ivoire, and this became the first reported case of EVD in West Africa [1]. Since this outbreak, West Africa went into epidemiologic silence, forgetting the situation that devastated a number of chimpanzees in the Taï National Park, Cote d'Ivoire, and subtly challenged the healthcare system in the sub-region. The routine surveillance system in West Africa (where it exists) does not include EVD or other filoviruses, and there is no documented report of monitoring for filoviruses in humans in the sub-region where malaria is endemic and often confused with other febrile diseases [2]. A total of 23 reported human outbreaks have occurred primarily in Central and Eastern Africa (six in the Democratic Republic of Congo, five in Uganda, four in Gabon, four in the Republic of Congo, three in South Sudan, and one each from Cote D'Ivoire and Guinea) [3]. In addition, 51 outbreaks and documented reports have been recorded in wild animals, with the last six reported from Ghana [4,5].

In addition to the first documented outbreak of Ebola in humans in 1976, previous re-evaluation of the yellow fever case of 1972 had revealed Ebola antibodies five years later [6]. Historically, case fatality rates (CFRs) have ranged from 41% to 89% (mean, 78%). The rapidity and intensity of control and the strains of the etiological agent (Zaire Ebola virus [ZEBOV] > Sudan Ebola virus [SEBOV] > the Bundibugyo Ebola virus [BEBOV] > Taï Forest Ebola) influenced the CFRs [7,8]. To date, three Ebola viruses have caused relatively large outbreaks in

humans in Africa, including the ZEBOV (13 outbreaks), SEBOV (7 outbreaks), and BEBOV (2 outbreaks) [9-11].

Description of the current outbreaks within West Africa, 2014

A two-year old boy died of EVD in Guéckédou, Guinea, on 6 December 2013 [12]. This incident resulted in other deaths, widespread devastations, and rapid dissemination to other territories within the country [7,12]. By the last week of March and early April 2014, respectively, the contiguous countries of Liberia and Sierra Leone had been infected [12]. Despite the international boundaries that exist in West Africa, the countries mentioned all belong to the same epidemiologic cluster and have similar health profiles [13,14].

The after-effect of wars in Guinea (2014 human population projection = 11,745,189), Liberia (2014 human population projection = 4,294,077), and Sierra Leone (2014 human population projection = 6,092,075) [15] weakened the health and laboratory services, and this caused delays in effective diagnosis and prompt emergency actions. In addition, the socio-cultural practices associated with burials – including the washing of corpses without ascertaining the cause of death – may facilitate infection transmission. Other factors that have been thought to play roles in the ongoing outbreaks and spread include poor risk communications, fears and social distancing of the sick, and ineffective infection controls with porous borders and overwhelmed laboratory and health services [6,16].

Currently, the following countries have been declared to be at the greatest risk of Ebola infection: Benin, Burkina Faso, Côte d'Ivoire, Guinea-Bissau, Mali, and Senegal [17]. In addition, the internationalization and huge interconnectedness of air and land travel, breaking of geographical barriers, poor health services in other countries, labor migrations, internal and external displacement of individuals, weak border controls, and lack of emergency preparedness expose many other African countries (and indeed other countries outside Africa) to the risk of contracting infection from contiguous and distantly infected locations.

On 20 July 2014, an Ebola-infected air traveller from Liberia entered into Lagos, Nigeria, via Togo and collapsed at the airport with symptoms of fever, vomiting, and diarrhea [18]. He subsequently died in a private hospital in Lagos, and 19 confirmed cases plus one probable case were linked to him, resulting in a total of eight deaths [19]. Similarly, on 30 August 2014, the Senegalese Health Authority reported the case of a 21-year-old male native of Guinea who travelled to Dakar, Senegal, by road, became symptomatic with EVD, and sought hospitalization on 23 August 2014. He was confirmed with fever, diarrhea, and vomiting, but subsequent confirmation for EVD was done on 26 August 2014 [20]. These countries have since been declared free of Ebola [21,22]. At the time of reporting, a single case and death of an Ebola patient imported from Guinea has been reported in a two-year-old girl in Mali [23]. Outside the African continent, recent Ebola outbreaks have been reported in the United States and Spain, among others [24,25]. As such, no country is immune to the global challenge of widespread dissemination of EVD.

While arguments may exist to support possible human introduction of the virus into West Africa, such arguments are weak because the dangerous human incursion into previously uninhabited portions of the forest may have facilitated current infections and transmissions [26,27]. Bausch and Schwarz [26] have also argued that ZEBOV may have existed in the West African sub-region for some time but was not detected by the surveillance systems. A recent work of Schoepp *et al*. provided more serological evidence of Ebola and other filoviruses than was previously diagnosed in Sierra Leone [27]. Hence, it is convenient to assume that the current trans-national infections with EVD in West Africa were facilitated by human activities and movements as observed in Nigeria, Senegal, and Mali [19-22].

In this work, we analyzed the current outbreaks of EVD in parts of West Africa and evaluated the risk of dying among infected patients based on certain epidemiological criteria.

Methodology

The historic and documented outbreaks of EVD due to Zaire Ebola virus since 1976 (Table 1, Supplementary Figure 1) were collected and reviewed. Meta-analysis of the CFRs of historic outbreaks and proportion of fatal cases (PFC) of current outbreaks was carried out on all cases due to ZEBOV to date using the random effects model [28]. All available data from the World Health Organization (WHO) website as submitted by the health authorities of affected countries [6,29,30] were collected. The inclusion criteria included all cases of EVD reported to the WHO or found on the Centers for Disease Control and Prevention (CDC) website that were confirmed by

at least one other report or peer-reviewed material. Duplicate cases were excluded as much as possible unless they were part of an earlier or incomplete report that was later upgraded. Exclusion criteria were cases of EVD due to other viruses apart from ZEBOV and experimental studies and reports found without confirmation. Using freely available epidemiologic software programs OpenEpi and Graphpad Quickcalc [31,32], descriptive statistics including incidence rates, case and mortality ratios, trends, percentages, and other useful epidemiological parameters were conducted. The risk of dying among patients infected with ZEBOV was evaluated based on gender, population groups, level of intensification of infections with ZEBOV in affected countries, bed capacities in designated hospitals in affected countries, transmission trends, and timelines of declaration by the WHO. Outputs are presented as tables and graphs.

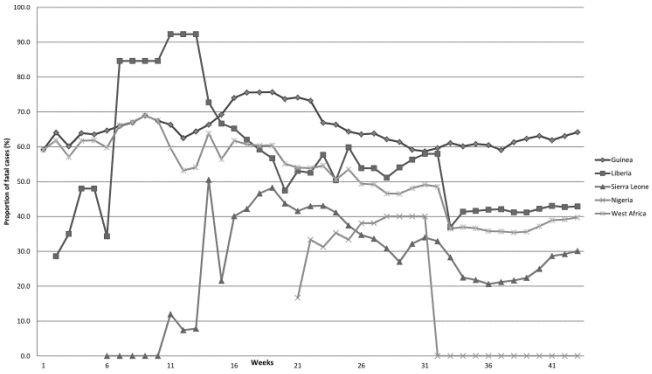
Results

Using weighted average of the random effects and based on the historical outbreaks to date, the mean case fatality rate and proportion of fatal cases from EVD caused by ZEBOV was 76.40% (95% CI = 68.0–84.8; 20 studies) (Table 1, online appendix 1). The heterogeneity among the outbreaks was 5.103 and the variability was 0.065. A total of 20,747 cases occurred as of 7 January 2015, and approximately 13.3%, 39.3%, and 47.1% of all cases to date in the ongoing outbreaks originated from Guinea, Liberia, and Sierra Leone, respectively; similarly, proportional deaths from Guinea, Liberia, and Sierra Leone were 21.6%, 42.5%, and 35.8% of all deaths (n = 8,235), respectively.

Nigeria and other affected countries accounted for approximately 0.3% of all cases and 0.1% of all deaths, while the countries with intense transmissions (Guinea, Liberia, and Sierra Leone) accounted for 99.7% of all cases and 99.9% of all deaths as of 7 January 2015 (Figures 1 & 2, online appendices 2 & 3). The PFC for all cases in West Africa (confirmed, probable, and suspected) peaked at 68.9% in week 9 of the epidemic (12–18 April 2014) but currently stands at 39.7% (95% CI = 39.0–40.4; n = 8,234/20,741) as of 7 January 2015.

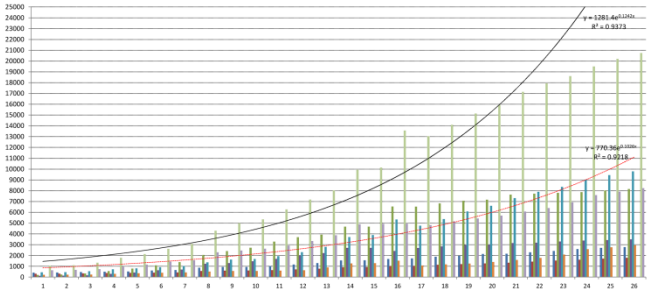
The months of May to July 2014 appeared to be the period of worst epidemics in terms of peaked PFC for West Africa, and a downward trend has persisted since that period. However, individual countries, especially Sierra Leone, have observed a surge in cases and deaths in recent days (Figure 1). The overall cumulative numbers of cases and deaths grew at

Figure 1. Patterns of cumulative percentage case fatalities in four of the affected West African countries, 23 March to 7 January 2015.



The weekly series was as follows for all events and calculations: up to 23 March was taken as the first week, 24 to 29 March was taken as the second week, 30 March to 5 April was taken as the third week and subsequently. All data used in the calculations were obtained from the WHO websites (Global Alert and Response (GAR): Ebola virus disease (EVD) (http://www.who.int/csr/don/archive/disease/ebola/en/) and Ebola Response Roadmap Situation Report Updates (http://www.who.int/csr/disease/ebola/situation-reports/en/). Full dataset with graph are available as online appendix 1.

Figure 2. Disaggregated cumulative cases and mortalities due to Ebola viral hemorrhagic disease (EVD) in affected countries in West Africa with exponential trend lines for overall cases and mortalities 18 July 2014 to 7 January 2015.



Note: The cases and deaths were disaggregated to be able to include the trend lines for each separately. (* presumptive and confirmed) (Table). Presumptive cases are combinations of probable and suspect cases. The trend line is reliable if the value of the individual R^2 is ≈ 1.0. Full dataset with graph are available as online appendix 3.

exponential rates until the end of June before the trends began to reduce slightly on a monthly basis, and as of 7 January 2015, the exponential values for the trend lines for cases and deaths stood at $y = 86.891e^{0.1416x}$ and $y = 61.457e^{0.1264x}$, respectively (Figure 2). The weekly incidences of new cases and deaths have been on the increase, especially since the declaration of health emergency and "out-of-control" situation by the WHO in week 22 (11–17 August 2014) [33] (Figure 3, online appendix 4).

Table 1. Meta-analysis of the proportion of fatal cases of Ebola virus disease outbreak caused by Zaire Ebola virus, 1976–2014

Study	Deaths	Sample size (cases)	Outcome (es)	SE	Var	w	w*es	w*(es^2)	w^2	w_v	w_v*es	w_v*(es^2)	w_v^2
WHO Ebola Response Team, 2014	1,656	2,250	0.736	0.018086213	0.000327111	3057.065	2250	1656	9345647.743	13.97045971	10.282258	7.56774214	195.17374
WHO, 1976, CDC, 2014	280	318	0.8805031	0.052620127	0.002768878	361.1571	318	280	130434.4818	13.50961169	11.895256	10.4738099	182.50961
Kuhn *et al*., 2011	32	52	0.6153846	0.108785659	0.01183432	84.5	52	32	7140.25	12.03560407	7.4065256	4.5578619	144.85577
Kahn *et al*., 1999; CDC, 2014; Kuhn *et al*., 2011	250	317	0.7886435	0.049878197	0.002487834	401.956	317	250	161568.6259	13.56110029	10.694874	8.43444325	183.90344
Georges *et al*., 1999; CDC, 2014	21	37	0.5675676	0.123853397	0.015339664	65.19048	37	21	4249.798186	11.54838977	6.5544915	3.72011679	133.36531
Kuhn *et al*., 2011	46	62	0.7419355	0.109392419	0.011966701	83.56522	62	46	6983.145558	12.0164583	8.9154368	6.61467892	144.39527
Kuhn *et al*., 2011	97	124	0.7822581	0.079426273	0.006308533	158.5155	124	97	25127.1523	12.89307313	10.08571	7.88962832	166.23133
CDC, 2014; Formenty *et al*., 2003	128	143	0.8951049	0.079116843	0.006259475	159.7578	143	128	25522.55865	12.90123327	11.547957	10.3366329	166.44182
Kuhn *et al*., 2011	10	11	0.9090909	0.287479787	0.082644628	12.1	11	10	146.41	6.497847273	5.9071339	5.37012171	42.222019
WHO, 2004; CDC, 2014	29	35	0.8285714	0.153861852	0.023673469	42.24138	35	29	1784.334126	10.53452561	8.7286069	7.23227431	110.97623
Kuhn *et al*., 2011	9	11	0.8181818	0.272727273	0.074380165	13.44444	11	9	180.7530864	6.866591599	5.6181204	4.59664396	47.15008
WHO, 2007; CDC, 2014	187	264	0.7083333	0.051798463	0.002683081	372.7059	264	187	138909.6747	13.52528864	9.5804128	6.78612572	182.93343
WHO, 2009	15	32	0.46875	0.12103073	0.014648438	68.26667	32	15	4660.337778	11.6413172	5.4568674	2.55790661	135.52027
CDC, 2014; WHO, 2014	7,588	19,497	0.3891881	0.004467822	1.99614E-05	50096.6	19497	7588	2509669440	15.37879127	5.9852423	2.32938494	236.50722
Fomenty *et al*., 2003	128	143	0.8951049	0.079116843	0.006259475	159.7578	143	128	25522.55865	12.90123327	11.547957	10.3366329	166.44182
WHO, 2003	43	57	0.754386	0.115042781	0.013234841	75.55814	57	43	5709.03245	11.83609337	8.9289827	6.73589924	140.09311
Akinveyeva *et al*., 2005	1	1	1	1	1	1	1	1	1	0.933486741	0.9334867	0.93348674	0.8713975
Borisevich *et al*., 2006	1	1	1	1	1	1	1	1	1	0.933486741	0.9334867	0.93348674	0.8713975
WHO, 1996	1	2	0.5	0.5	0.25	4	2	1	16	3.112816293	1.5564081	0.77820407	9.6896253
Kuhn *et al*., 2011	1	1	1	1	1	1	1	1	1	0.933486741	0.9334867	0.93348674	0.8713975
			0.7639502										
k	20				Sums:	55,219.38	23,358	10,523	2,519,553,046	212.1213406	154.49615	117.628731	2768.0199
df	19	**Proportion of fatal cases (PFC) ≈ 76.40% (95% CI = 68.03–84.76)**											

SE: standard error; Var: variance; w: study weight; w*es: weight effect size; w_v: new weight for each study; w_v*(es2): new weight effect size; k: number of studies/observations; df: degree of freedom; Q_v = 5.103 (heterogeneity among the studies); I^2_v = -272.314 (heterogeneity quantification); es = 0.728 (95% CI = 0.594–0.863) (effect summary); v = 0.065 (variability); SEes = 0.069 (standard error effect summary).

Table 2. Risk of death among Ebola virus disease patients, 23 March to 7 January 2015

Variable	Descriptor	Total	Risk of death (%)	95% CI	Odd ratio	Overall risk (%)	Risk ratio	χ^2	P value (2-tailed)	References
Gender	Male	685	75.2	71.8–78.3	1.1	74.6	1.0	0.2	0.64	[37]
	Female	730	74.1	70.8–77.2	Ref	-	-	-	-	
Population group	Healthcare workers	649	55.3	51.5–59.1	1.9	39.5	1.4	70.7	< 0.001	[52]
	General population	19,497	38.9	38.2–39.6	Ref	-	-	-	-	
Three intensely affected countries	Sierra Leone	7,017	31.6	30.5–32.7	Ref	-	-	-	-	[52,53]
	Guinea	2,284	58.8	56.8–60.9	3.1	38.3	1.9	542.1	< 0.001	[52,53]
	Liberia	7,862	43.0	42.0–44.1	1.6	37.6	1.4	207.5	< 0.001	[52,53]
Bed capacity at ETC	Sufficient[≠]	1,318	58.9	56.2–61.5	1.7	48.4	1.3	70.0	< 0.001	[7,20,23-25,33,34,54]
	Insufficient	6,713	46.3	45.1–47.5	Ref	-	-	-	-	
Transmission trend	Intense/widespread	8,013	48.1		1.4	48.1	1.2	0.5	0.47	[52,53]
	Localized	20	40.0	21.8–61.4	Ref	-	-	-	-	
Timeline from WHO declaration[∞]	Before declaration	1,814	55.8	53.6–58.1	1.5	48.1	1.2	56.1	< 0.001	[37,52,53]
	After declaration	6,219	45.9	44.6–47.1	Ref	-	-	-	-	

ETC: Ebola treatment centre; [≠] Sufficient bed capacity means that the country meets at least 75% of it need in terms of bed capacity. Based on the report of 8 October, Guinea has met 76%, Liberia 21%, Sierra Leone 26%, and Nigeria > 100% of the bed capacity needs; [∞]The WHO declared EVD in West Africa an out-of-control public health emergency of international concern on 8 August 2014 [43]. The WHO declaration was accompanied by intense mass mobilisation in the infected countries. Strengthening of bed capacities was accompanied by improved laboratory services, strengthened surveillance, and safe burial practices. Intense/widespread transmission countries are Liberia, Guinea, and Sierra Leone; Nigeria has localized infections.

Table 3. Situation of cumulative cases and mortalities in healthcare workers as at 7 January 2015

	West Africa			Guinea			Liberia			Sierra Leone		
Date	Cases	Deaths	PFC (%)	Cases	Deaths	PFC (%)	Cases	Deaths	PFC (%)	Cases	Deaths	PFC (%)
14 Sep	318	151	47.5	61	30	49.2	172	85	49.4	74	31	41.9
21 Sep	373	208	55.8	67	35	52.2	182	87	47.8	113	81	71.7
28 Sep	377	216	57.3	67	35	52.2	185	95	51.4	114	81	71.1
05 Oct	401	232	57.9	73	38	52.1	188	94	50.0	127	95	74.8
12 Oct	427	236	55.3	78	40	51.3	209	96	45.9	127	95	74.8
19 Oct	443	244	55.1	80	41	51.3	222	103	46.4	127	95	74.8
23 Oct	446	244	54.7	80	41	51.3	228	103	45.2	127	95	74.8
29 Oct	517	272	52.6	80	43	53.8	299	123	41.1	127	101	79.5
05 Nov	542	310	57.2	88	46	52.3	315	157	49.8	128	102	79.7
12 Nov	549	315	57.4	92	51	55.4	329	162	49.2	128	102	79.7
19 Nov	568	329	57.9	95	55	57.9	341	170	49.9	132	104	78.8
26 Nov	575	333	57.9	97	56	57.7	342	172	50.3	136	105	77.2
03 Dec	605	339	56.0	106	59	55.7	361	174	48.2	138	106	76.8
10 Dec	622	342	55.0	121	62	51.2	363	174	47.9	138	106	76.8
17 Dec	632	358	56.6	125	72	57.6	365	177	48.5	142	109	76.8
24 Dec	649	359	55.3	139	72	51.8	367	177	48.2	143	110	76.9
31 Dec	660	375	56.8	148	87	58.8	369	178	48.2	143	110	76.9
7 Jan 15	820	488	59.5	154	89	57.8	370	178	48.1	296	221	74.7

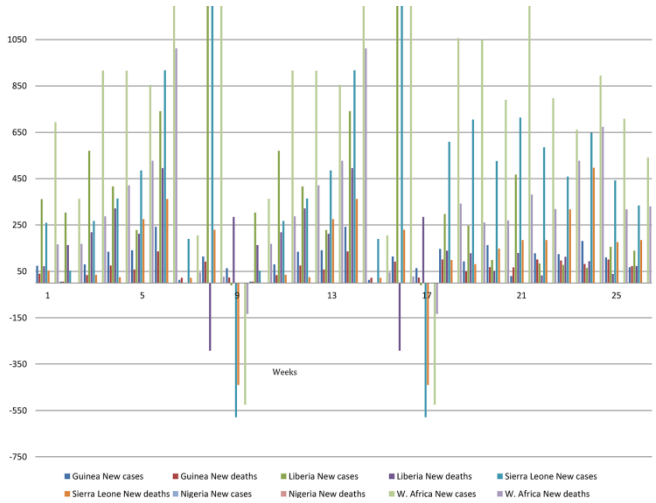
PFC: proportion of fatal cases

No difference was observed between the risk of dying among infected male and female patients (Table 2). However, healthcare workers were at a slightly higher risk of dying due to EVD compared with the general populace. The risk of dying among EVD patients was generally higher in Guinea and Liberia than in Sierra Leone. The risk of dying among the patients was also higher in intense transmission countries than in countries with localized or isolated infections. Similar risk was observed in countries with sufficient bed capacities compared with those with insufficient bed capacities (Table 2). Since the time of declaration of health emergency and "out-of-control" situation by the WHO on 8 August 2014 [33], there was an observed reduced risk of dying among infected patients (Table 2). As at 7 January 2015, approximately 59.5% (95% CI = 56.1–62.8; n = 488/820) of the infected healthcare workers had died cumulatively, but significantly more deaths were recorded in healthcare workers in Sierra Leone (74.7%; 95% CI = 69.4–79.3) than in Guinea (57.8%; 95% CI = 49.9–65.3) or Liberia (48.1%; 95% CI = 43.1–53.2) ($p < 0.0001$, Table 3). Overall, the cumulative trends of deaths among healthcare workers appeared to be on the increase in the affected countries and are particularly worrisome in recent times in Sierra Leone.

Discussion

We evaluated the ongoing outbreaks of EVD in West Africa and outlined some important epidemiological concepts associated with the current ZEBOV infections. The current outbreaks remain the largest episodes of EVD to date. Though the precursor virus caused infection in Guéckédou, a remote area of Guinea, on 6 December 2013, the resulting infections remained localized in four local communities, similar to what was found in most of the past outbreaks until 30 March 2014 [12,34,35]. The internationalization of this outbreak and the spread to the contiguous countries of Liberia and Sierra Leone changed the dynamics of these outbreaks. To date, a total of nine countries have been infected, including Guinea, Liberia, Sierra Leone, Mali, Nigeria, Senegal, Spain, the United Kingdom, and the United States. In this report, we calculated the mean CFR/PFC of all EVD caused by ZEBOV to date to be 76.3% (95% CI = 67.8–84.8). The use of PFC to replace CFR as a measure of risk of death in the ongoing outbreak was previously explained by Majumder [36]. Since the final outcome of the current outbreaks is not known and the dynamics of CFR can change daily as the course of the disease progresses, the use of PFC for the ongoing outbreaks interchangeably with CFR for concluded outbreaks is appropriate. This CFR/PFC value obtained in this report is comparable to the CFR from previous reports, including 78% (99.5% CI = 71%–84%) [8], 50%–90%, [37], and 70.8% (95% CI = 69%–73%) for patients with known clinical outcomes in the ongoing outbreak [38].

Figure 3. Incidence of new cases and mortalities of EVD per week, West Africa (trend from 18 July 2014 to 7 January 2015).



Negative values: Number of cases or deaths was reviewed downward due to reclassification, retrospective investigation, consolidation of cases and laboratory data, and enhanced surveillance that did not confirm Ebola viral hemorrhagic disease (EVD) as the cause of the disease or death. Yellow highlights are current week values that may change weekly. Full dataset with graph are available as online appendix 2.

The cases in Liberia and Sierra Leone have almost quadrupled and tripled, respectively, the number of cases in Guinea, where the current outbreaks began. To date, approximately 150, 75, and 13 persons per 100,000 population have been infected, respectively, in Liberia, Sierra Leone, and Guinea [39].

While outbreaks have been massive in these three countries (Guinea, Liberia, and Sierra Leone), limited and local outbreaks have been reported and contained in Nigeria, Senegal, Mali, and elsewhere outside the continent. It has been confirmed that these intensely affected countries have weakened health and laboratory services, delayed effective diagnosis, and slow emergency responses in addition to national apathy, denialism, and unpreparedness [13,40,41]. The effectiveness of prompt and rapid diagnostic services, timely contact tracing, and good health service systems cannot be underestimated in the situation of rapid containment despite the lack of unpreparedness in other African countries [19,41]. For example, had

the index case not become symptomatic and detected in the airport in Nigeria, he may have gone into a city with a population of approximately 21 million or travelled further within Nigeria en route to the United States with consequent multiple contacts. A similar situation may have occurred in Senegal and Mali had the index cases not been promptly removed from the larger populations. It is possible that the rapid containment and subsequent limited spread observed in the six other countries that were infected after the first three benefitted tremendously from the lesson of prompt action. The effects of delayed diagnosis have been established in previous works [19,42,43]. There is therefore a need to improve disease monitoring and health systems in African countries. The responsible governments of African countries will need to build capacities for more competent staff by effectively equipping laboratories across the continent for effective diagnosis of viral hemorrhagic fevers (VHFs), including Ebola. The WHO and health policymakers will need to reassess the spread of the WHO Emerging and Dangerous Pathogens Laboratory Network [44]. The current geographical spread shows that four out of the five such laboratories in Africa are located in Central, East, and Southern Africa [44]. The only laboratory in heavily populated West Africa is situated in Dakar, Senegal, with none in the Northern part of Africa. With a surging human population, the human and animal health challenges, and the lingual dichotomy in the West Africa sub-region, many more such laboratories will need to be established by improving the capacities of some existing potential facilities that can fulfill such stringent conditions for the approval of other biosafety level 4 laboratories.

Previously, at the closing ceremony of the WHO-led team of experts on the control of Ebola in the Kikwit in 1995, an African scientist (Oyewale Tomori) had emphasized that part of the international funds raised to contain the Ebola epidemic at that time be disbursed to upgrade the uncompleted P3-level biosafety laboratory in Kinshasa that had been abandoned by the French government. Such a laboratory would add to the current facilities and enhance the capacity of African scientists to provide support for disease surveillance and enable them in the future to rapidly handle outbreaks. Though the advice was ignored back then due to other priorities, it has now becomes more necessary than ever before. According to Tomori, if the Kinshasa lab and other such facilities are not supported and another Ebola epidemic occurs in another 10 or 20 years in any African country, that country would call for external help, to the detriment of the local scientists; thousands of human deaths will possibly occur again (Tomori, personal communication).

While the current outbreaks are the largest to date of all EVD outbreaks to date (at least > 20,000 individual case counts as of 31 December 2014, Figure 2), the contributions of delayed response in the early course of the epidemics will need to be specifically analyzed. These outbreaks presented with a worst-case scenario in the period between May and June 2014, with PFC in some cases approaching 100% (Figure 1); during the same period, the doubling time of between 15.7 days (Guinea) and 30.2 days (Sierra Leone) existed in the field [38].

The epidemiologic situation appears to be improving but data gaps exist, with the worst situation in data gathering occurring in Liberia, especially when the healthcare workers were on strike. At the moment, more needs to be done and it will appear that since the time of declaration of health emergency and "out-of-control" situation by the WHO on 8 August 2014, there appear to be some reduced risks of dying among hospitalized patients (Table 1), and the exponential trends have begun to drop slightly (Figure 2). However, the same period coincided with records of increased numbers of new cases. A combination of factors may have been responsible for the above observations. It is likely that following this declaration, there was an improved international response to the situation in the affected countries, more healthcare workers enrolled for interventions, there were improved rates of diagnosis and detection, more patient sought hospitalization, bed capacities increased, contact tracing was better, and so follow-ups became easier for case counts.

While gender difference has been observed in certain outbreaks of other infectious diseases [45], the analysis of the current outbreaks of Ebola does not support gender differences. The WHO Response Team [38] reached the same conclusion in its evaluation of the ongoing outbreaks. However, some non-peer-reviewed media reports have stated that more women than men have been infected in the ongoing outbreaks [46]. In addition, infected healthcare workers are at a higher risk of dying compared with the general population. The Centers for Disease Control and Prevention in the United States has confirmed that EVD among healthcare personnel and other persons is associated with direct contact with infected persons, bodies of persons who died from EVD, direct contact with bodily fluids from EVD patients [47], and, in addition, the inadequacies of personal protective

equipment. Similarly, since the beginning of records of outbreaks and deaths in healthcare workers, there has been an increasing trend in cumulative deaths, especially in Sierra Leone. The reason for this observation will need further evaluation.

We identified the risk of dying as higher in intense-transmission countries and in countries with sufficient bed capacities in the treatment centres. While it is understandable that the intense-transmission countries may have higher numbers of cases and greater risk of dying among EVD patients due to scarce and overstretched health facilities and the level of exposure or contacts, the increased risk of dying among patients in countries with sufficient bed capacities may be linked to higher chances of hospitalization, monitoring, and adequacy of case and death records. It has been suggested that underreporting has played a huge role in the ongoing outbreaks [42,48,49].

Our analyses are subject to certain limitations. Records are often incomplete or lacking in an outbreak situation, and censorship and multiple revisions of case and death counts may be present in the ongoing outbreak. In addition, definitive outcomes of some cases were not yet known, and probable and suspected cases were included in our analyses. Finally, underreporting has been confirmed in some cases. These played some role in the epidemic curve and incidence of new cases and deaths produced in this analysis, where some degrees of downward trends were observed in the last few weeks of epidemics (up to 5 November). It must be emphasised that the healthcare workers in Liberia were also on strike at about this time, which impacted documented records (Figures 2 and 3) [49,50]. The careful coordination of epidemiological data in the face of health emergencies becomes obvious and necessary.

Conclusions

Africa has not been able to contain any of the outbreaks of EVD since 1976 alone, but it has become powerless, confused, disoriented, and totally helpless, resorting to international aid each time. The 2013–2015 West African outbreak has been designated as "an "out-of-control" public health emergency of international concern on August 8 2014 by the WHO [33]. Several factors, including the deplorable health infrastructure and a loss of confidence in public healthcare, enhance the spread and magnitude of this outbreak.

External experts have used these outbreaks to fine-tune their capability for epidemic control elsewhere outside Africa, and African researchers should learn from this situation. Dependency on external help opens new possibilities of large-scale transboundary transmission of such pathogens like Ebola, and had recently become a subject of heated debate in the United States when two American aid workers returned to the United States for treatment following their infection with Ebola in Africa [51].

Though a previous report predicted higher case numbers (≥ 20,000 cases by 2 November 2014) [38], intensification of surveillance, improved diagnostic efforts, increased volunteering of healthcare staff, and enhancement of health facilities in the intensely affected countries have had a positive effect on reducing projected cases. A much graver estimate (≈ 500,000 in Liberia and Sierra Leone by 20 January 2015) [42] was unrealistic with the current trend.

Footnote

Since the time of conducting this analysis and submitting this report, the outbreak figures have risen to 25,826 cases and 10,704 deaths (WHO Ebola Roadmap Situation Report of 15 April 2015).

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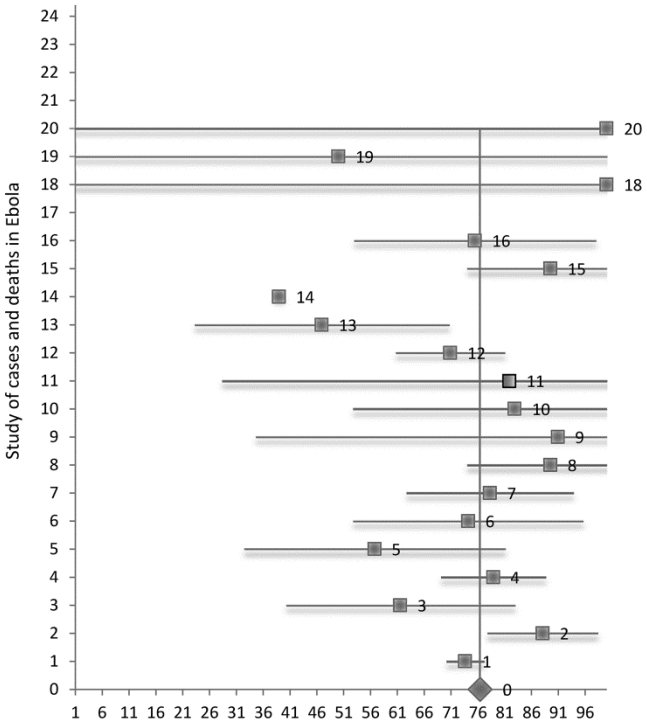
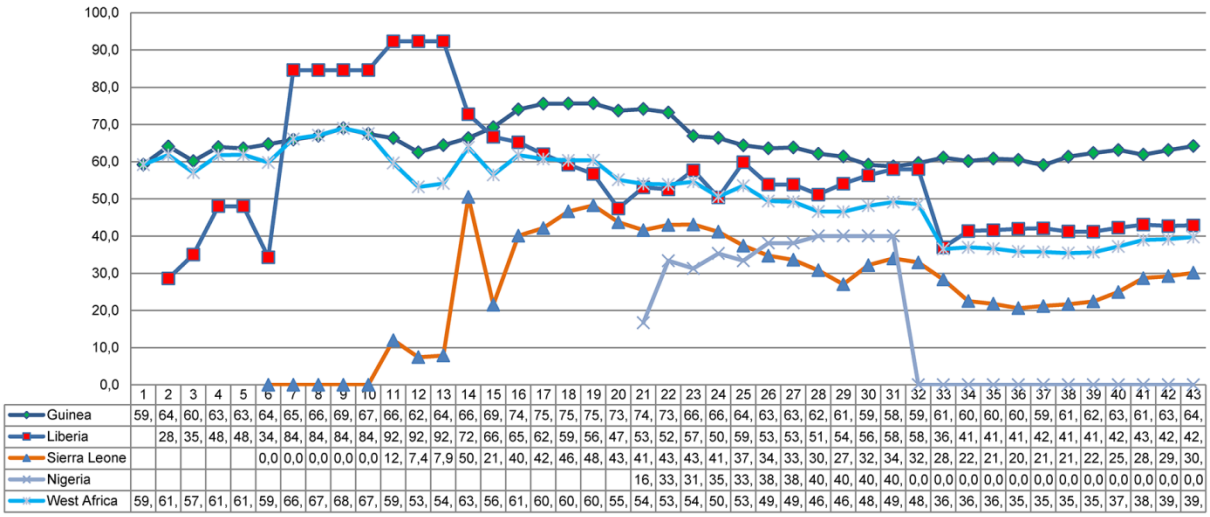
Supplementary items

Supplementary Figure 1. Forest plot of proportion of fatal cases of Ebola virus disease outbreak caused by Zaire Ebola virus, 1976–2014.

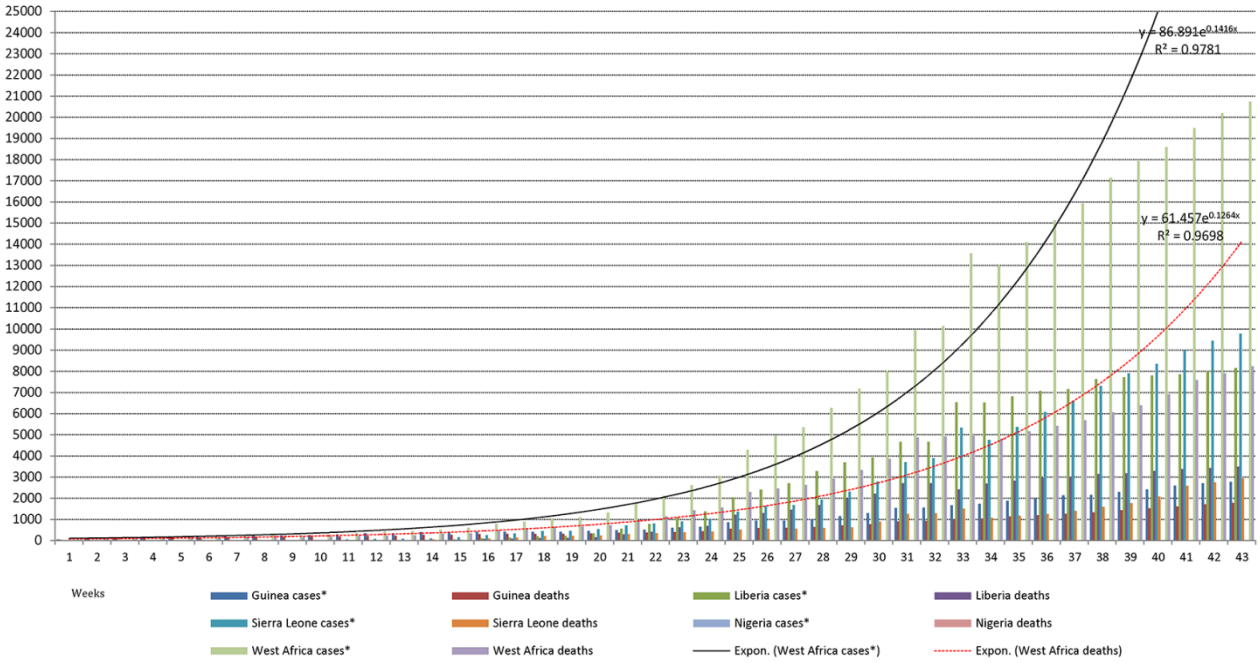


Supplementary Figure 2. Complete details of proportion of fatal cases of Ebola virus disease, West Africa, 23 March



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43
Guinea	59,	64,	60,	63,	63,	64,	65,	66,	69,	67,	66,	62,	64,	66,	69,	74,	75,	75,	75,	73,	74,	73,	66,	66,	64,	63,	63,	62,	61,	59,	58,	59,	61,	60,	60,	60,	59,	61,	62,	63,	61,	63,	64,
Liberia		28,	35,	48,	48,	34,	84,	84,	84,	84,	92,	92,	92,	72,	66,	65,	62,	59,	56,	47,	53,	52,	57,	50,	59,	53,	53,	51,	54,	56,	58,	58,	36,	41,	41,	41,	42,	41,	41,	42,	43,	42,	42,
Sierra Leone						0,0	0,0	0,0	0,0	0,0	12,	7,4	7,9	50,	21,	40,	42,	46,	48,	43,	41,	43,	43,	41,	37,	34,	33,	30,	27,	32,	34,	32,	28,	22,	21,	20,	21,	21,	22,	25,	28,	29,	30,
Nigeria																					16,	33,	31,	35,	33,	38,	38,	40,	40,	40,	40,	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
West Africa	59,	61,	57,	61,	61,	59,	66,	67,	68,	67,	59,	53,	54,	63,	56,	61,	60,	60,	60,	55,	54,	53,	54,	50,	53,	49,	49,	46,	46,	48,	49,	48,	36,	36,	36,	35,	35,	35,	35,	37,	38,	39,	39,

Supplementary Figure 3. Disaggregated cumulative cases and mortalities due to Ebola viral hemorrhagic disease (EVD) in affected countries in West Africa with exponential trend lines for overall cases and mortalities 23 March 2014 to 7 January 2015



Supplementary Figure 4. Incidence of new cases and mortalities of EVD per week, West Africa (trend from 18 July 2014 to 7 January 2015).