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# Ebola outbreak in rural West Africa: epidemiology, clinical features and outcomes

Silvia Dallatomasinas<sup>1</sup>, Rosa Crestani<sup>2</sup>, James Sylvester Squire<sup>3</sup>, Hilde Declerk<sup>2</sup>, Grazia Marta Caleo<sup>4</sup>, Anja Wolz<sup>2</sup>, Kathyrn Stinson<sup>1,5</sup>, Gabriela Patten<sup>1</sup>, Raphael Brechard<sup>6</sup>, Osman Bamba-Moi Gbabai<sup>3</sup>, Armand Spreicher<sup>2</sup>, Michel Van Herp<sup>2</sup>, Rony Zachariah<sup>7</sup>

- 1. Médecins Sans Frontières, Freetown, Sierra Leone
- 2. Médecins Sans Frontières, Ebola Task Force, Brussels Operational Centre, Brussels, Belgium
- 3. Ministry of Health and Sanitation, District Health Services, Kailahun, Sierra Leone
- 4. Manson Unit, Médecins Sans Frontières, London, United Kingdom
- 5. University of Capetown, Capetown, South Africa
- 6. Médecins Sans Frontières, Freetown, Sierra Leone
- 7. Médecins Sans Frontières Operational Research Unit, Brussels Operational Centre, Luxembourg

# ABSTRACT

**Objective:** To describe Ebola cases in the district Ebola Management Centre of in Kailahun, a remote rural district of Sierra Leone, in terms of geographic origin, patient and hospitalization characteristics, treatment outcomes and time from symptom onset to admission.

**Methods:** Data of all Ebola cases from June 23<sup>rd</sup> to October 5<sup>th</sup> 2014 were reviewed. Ebola was confirmed by reverse-transcriptase-polymerase-chain-reaction assay.

**Results:** Of 489 confirmed cases (51% male, median age 28 years), 166 (34%) originated outside Kailahun district. Twenty-eight (6%) were health workers: 2 doctors, 11 nurses, 2 laboratory technicians, 7 community health workers, and 6 other cadres. More than 50% of patients had fever, headache, abdominal pain, diarrhoea/vomiting. An unusual feature was cough in 40%. Unexplained bleeding was reported in 5%. Outcomes for the 489 confirmed cases were: 227 (47%) discharges, 259 (53%) deaths, and 3 transfers. Case fatality in health workers (68%) was higher than other occupations (52%, P= 0.05). The median community infectivity time was 6.5 days for both general population and health workers (P=0.4)

**Conclusions:** One in three admitted cases originated outside Kailahun district due to limited national access to Ebola Management Centers - complicating contact tracing, safe burial and disinfection measures. The comparatively high case fatality among health workers requires attention. The community infectivity time needs to be reduced to prevent continued transmission.

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### INTRODUCTION

Ebola virus disease (EVD), also called Ebola Haemorrhagic Fever or simply Ebola, is a disease of humans and other primates caused by viruses of the family filovaridae. It was first discovered in 1976 close to the Ebola River in the Democratic Republic of Congo from which it gets its name. Fruit bats are believed to be the virus reservoir, able to spread the virus without being affected. Humans become infected by contact with bats or a living or dead animal that has been infected by bats. This then leads to human outbreaks. Casefatality can be as high as 90% and despite four decades of documented existence there is no specific licenced treatment for Ebola. It is thus considered a Neglected Tropical Disease.

The incubation period lasts 2 to 21 days and pathogenesis involves immune suppression and a systemic inflammatory response that causes impairment of the vascular, coagulation and immune systems, leading to multiorgan failure. Virus transmission during outbreaks occurs through transmission in the community between household members, close contacts and caregivers of Ebola patients; contact with dead bodies or body fluids during funeral ceremonies; and in health facilities through breaches in barrier nursing and contamination of medical equipment. The response comprises early diagnosis, isolation and supportive medical care for confirmed cases; contact tracing through daily surveillance of contacts; active case-finding and alert investigations; safe burial practices and home disinfection; and health promotion to ensure community acceptance of these measures. Ensuring that these activities are conducted in a safe manner requires staff to be trained in infection control and equipped with personal protective equipment.

On August 8, 2014 WHO declared the West African Ebola epidemic in Guinea, Liberia, Nigeria, Senegal and Sierra Leone a "public health emergency of international concern" - this being the largest outbreak in history. Sierra Leone is one of the worst-affected countries with a doubling of cases every 30 days as of September 2014.

Although WHO has analysed the epidemiologic characteristics of the outbreak using multi-country data from West Africa, no analysis has focused on a rural district setting. Knowledge of the epidemiologic characteristics of the outbreak in hard-to-reach rural areas with considerable logistic and resource challenges is vital to identify gaps in control efforts and inform an effective response. Since June 2014, Médecins Sans Frontières has managed the Ebola Management Centre in the rural district of Kailahun in Sierra Leone. During the first 4 months (June to October 2014) of the outbreak, we assessed trends in admissions of Ebola cases to the Ebola Management Center in terms of geographic mapping, patient and hospitalization characteristics, treatment outcomes, and community infectivity time.

# METHODS

This observational study in November 2014 included all patients who were enrolled consecutively at arrival at the Ebola Management Center between 23<sup>rd</sup> June and 5<sup>th</sup> October 2014. Follow-up was censured on 10<sup>th</sup>

### Study setting and site

Sierra Leone has an estimated population of six million and despite decades of mining of diamonds, titanium, bauxite and gold, 70% of its people live in poverty. The 1991 to 2002 civil war devastated the country and its health system; Sierra Leone ranks 5<sup>th</sup> highest for maternal mortality and 11<sup>th</sup> for infant mortality worldwide. Even before the Ebola outbreak, which resulted in the deaths of many health workers, there were only 0.2 doctors and 1.7 nurses per 10,000 population, mostly located in urban areas. The study site was the only Ebola Management centre in Kailahun town in rural Kailahun district of Sierra Leone, which has 400,000 inhabitants and a surface area of 4,859 km<sup>2</sup>. It lies in the north east of Sierra Leone and is bordered by Liberia to the east and Guinea to the north.

### Ebola control at district level

The district health management team of the Ministry of Health and Sanitation is responsible for overall coordination of Ebola control activities and partners. Partners include the International Federation of the Red Cross (involved with safe burials and home disinfection), Save the Children (contact tracing), WHO (safe burials, support to contact tracing, surveillance, logistic support and training), the World Food Programme (providing food for households under quarantine), the National Microbiological Laboratory, Winnipeg, Canada (laboratory diagnosis of Ebola), and MSF (management of the Ebola Management Center, health promotion). A national Ebola call centre receives alerts and despatches teams to investigate and implement control activities. This includes investigating alerts of suspect cases and deaths in the community. At the time of this report, only 3 dedicated ambulances were available in the whole district for patient transfers to the Ebola Management Center.

### The MSF Ebola Management Centre.

Confirmed and suspected Ebola cases from Kailahun and those referred from neighbouring districts were admitted to the Ebola Management Center, which progressively increased its bed capacity from 72 to 94 beds. The setup and functioning of the centre has been previously described (au: reference??). In brief, approximately 25 people per day - doctors, nurses, disinfection teams, cooks, cleaners, health promotion, counselling teams and logisticians - ensure six-hourly shifts. The centre has its independent water supply, 24-hour electricity supply and an on-site kitchen.

Patients arrive by ambulances and are assessed in a triage area. Their clinical signs are then recorded and they are admitted to the suspect or probable area of the centre depending on their case classification. All cases undergo on-site laboratory confirmation by Real Time Polymerase Chain Reaction (RT-PCR, Public Health Agency, Winnipeg, Canada). Confirmed Ebola cases are then moved to the confirmed area of the centre. Supportive care is provided until the PCR turns negative. Those with two negative PCR tests for Ebola are discharged to seek care from the general health services. All cases receive a systematic course of antimalarials, a broad-spectrum antibiotic and symptomatic care for fever, diarrhoea and vomiting.

Treatment outcomes were standardized and documented as: recovered (showed clinical improvement and was discharged PCR-negative); death after being admitted; abandoned (left without medical consent); transferred (transferred to another facility). A patient admitted as an Ebola suspect but found negative on repeated PCRs was classified as a non-case.

### Data collection and statistical analysis

An epidemiologist gathered data from patient files daily and encoded them into a password-protected database used for the analysis. Information on contacts was sourced from the District Health Office. Treatment outcomes for the period June 23<sup>rd</sup> to October 5<sup>th</sup> 2014 were censured on 10<sup>th</sup> November 2014.

The cumulative incidence of death was estimated and expressed graphically using the Kaplan-Meier method. The number of days from onset of symptoms to admission at the Ebola Management Center was considered the community infectivity time. Differences between groups were compared using chi-square and Wilcoxon Rank-sum test. The level of significance was set at  $P \le 0.05$  and 95% confidence intervals (CIs) were used. Data analysis was performed using STATA 11 software (Stata Corporation, Texas, USA).

## **Ethical considerations**

The study used data collected during surveillance and response activities for Ebola at district level and stripped of patient identifiers. Informed consent was not applicable. The study satisfied the MSF Ethics Review Board criteria for studies using routinely collected data (Geneva, Switzerland); the Ebola interventions were approved by the Ministry of Health, Sierra Leone.

# RESULTS

#### Trend in admissions and geographic origin of cases

Figure 1 shows the trend in admissions stratified by Ebola cases and non-cases. Of 709 patients admitted to the Ebola Management Center with clinical features suggestive of Ebola, 220 (31%) were declared non-cases after PCR testing and discharged (median hospitalisation time 2 days, IQR 1-3).

Figure 2 shows the upward and erratic trend in confirmed cases of Ebola admitted to the EMC. This trend is influenced by ambulance availability for referrals and cases from other districts. Figure 3 shows the widespread origin of Ebola cases from all over Sierra Leone. Of 489 confirmed cases, 166 (34%) originated from districts other than Kailahun - some as far as Freetown, 416 km and 8-9 hours away.

### **Patient characteristics**

Of 489 confirmed cases, 250 (51%) were male. The median age was 28 years (IQR, inter-quartile range: 17-40 years, range 3 months – 80 years). Only 3 individuals had eaten bush meat, while 76 (16%) had attended a funeral in the previous 21 days. The great majority (401) of cases were thus likely related to direct contact with body fluids of infected individuals at home or in the community.

Twenty-eight health workers were admitted with Ebola (19 from Kailahun district and 12 from other districts) comprising 11 nurses, 7 community health workers, 2 doctors, 2 laboratory technicians, an ambulance driver, a vaccinator, a WHO staff, a contact tracer, a counsellor, and a surveillance officer.

### **Clinical manifestations**

Table 1 shows the clinical features of 245 consecutive Ebola patients for whom clinical history was recorded consecutively from August 2014. Fever, fatigue, headache, joint and abdominal pains, diarrhoea and vomiting were present in >50%. Unusual features were chest pain in 44% and cough in 40%. Unexplained bleeding was seen in only 5%. The median hospitalisation time (Figure 4) for all 489 confirmed cases was 7 days (IQR 3-14, range 1-35). For patients who died this was 4 days (IQR 2-6, range 1-31), for patients who recovered, 14 days (IQR 11-19, range 4-35).

### Case fatality and treatment outcomes

Of the 489 admitted Ebola cases, one outcome was unrecorded in the database. Of the remaining 488, 227 (47%, 95% CI: 42-51) were discharged, 259 died (53%, 95% CI:49-58) ), and 3 (1%) were transferred.

Figure 5 shows the cumulative incidence of death among confirmed Ebola cases. 246 (95%) deaths occurred within the first 10 days of admission and 8 after 10 to 18 days. Five patients died after at least 18 days (including one at 31 days), when they were in the recovery or convalescent phase (defined as late deaths). Exact reasons for these late deaths are unknown.

Of the 28 health workers admitted, 19 (68%) died (2 doctors and 2 laboratory technicians, 7 of the 11 nurses, 3 of the 7 community workers, the ambulance driver, the vaccinator, a national staff working for an international organization, a counsellor and a surveillance officer). Case-fatality in health workers (68%, 95% CI: 48-84) was higher than in other occupations (52%, 95% CI: 47-57) (*P*= 0.05)

## Contact tracing and community infectivity time

In addition to 489 confirmed Ebola cases, there were 36 probable cases - 19 deaths on ambulance arrival and 17 unexplained community deaths. The number of contacts for all 525 cases was estimated at 5250, of whom 1923 (37%) were identified. The median community infectivity time (CIT) was 6.5 days (IQR 3-8 days) for both general population and health workers (*P*=0.4). Median CIT was 4 days (IQR, 3-7) for cases from Kailahun district and 8 days (IQR, 5-11) for those from other districts (P<0.001).

# DISCUSSION

This is the first study from a remote rural district setting in Sierra Leone during the current Ebola outbreak. It shows an upward trend in Ebola admissions with one in three cases originating from outside the district. Although about half of all admitted Ebola cases recovered, the case-fatality rate among health workers was high. Of particular concern is the long community infectivity time, which magnifies community transmission.

Our findings reflect the reality of a district setting with very limited logistics and few trained staff struggling to cope with the scale of the outbreak. It also points to inadequate infection control and protection of health workers within an already weak health system eroded by decades of conflict.

The data came from an operational setting and likely to reflect the ground reality; treatment outcomes were standardized and on-site epidemiologists collected the data. There was also ready access to Ebola laboratory testing, a key component in managing cases, and MSF has considerable experience in managing Ebola from previous epidemics. However, there is likely to be significant underreporting of cases for various reasons: Data on confirmed cases only included those were admitted to the Ebola Management Center but not those who could not be admitted when bed capacity was reached. Dire shortages of dedicated ambulances – three for a district population of almost half a million - meant that many cases never made it to the Ebola Management Center. Stringent government-mandated quarantine and resulting household food shortages reportedly led to hiding of possible Ebola cases, stigma, distrust and even hostility towards health workers. This complicated surveillance and identification of new clusters. Development of social acceptance through health promotion and careful collaboration with communities leading to understanding of anthropological perspectives is vital but was missed in the early stages of launching control interventions. Research in this area is urgently required (Bolten 2014).

Despite these limitations, our findings raise a number of important operational observations. First, more than one-in-three confirmed Ebola cases originated from outside Kailahun district since most districts did not have functioning Ebola Management Center. The community infectivity time was significantly higher for those originating from other districts, which fostered transmission. No formal coordination system for surveillance and reporting between districts existed. These shortcomings complicated contact tracing, safe burial procedures and disinfection measures at sites beyond the jurisdiction of a given district. Transportation of recovered patients and corpses to their homes was a challenge. An issue of serious concern to heath workers and the community at large was that burial of corpses from distant locations often occurred without the presence of loved ones. These problems highlight the necessity of having at least one Ebola Management Center in every district, something that still has not been achieved.

Second, a third of patients arriving at the Ebola Management Centre were noncases, putting them at potential risk of Ebola cross-infection. To avoid this, ambulances should not transport several patients at once, the quality of triage before admission must improve and partitions between patients in the suspect area must be introduced. Have a point-of-care rapid diagnostic test that excludes non-Ebola cases would considerably reduce unnecessary admissions, although probable cases who present early would still need to be admitted for a repeat PCR test after 48-72 hours.

Third, the unusual observation that almost half of all confirmed cases presented with a cough poses a risk of cross-infection due to droplet propulsion between patients and clinical staff during triage. Face masks need to be given to patients on arrival and protection measures for staff improved.

Fourth, the majority of deaths occurred within 10 days of admission when supportive therapy is likely to impact survival. Unfortunately, the scale of the epidemic, the very difficult working environment, and the need to ensure maximum safety for health workers limited the use of invasive procedures such as intravenous fluids and/or aggressive correction of electrolyte imbalances when the workload became high. Innovative ways of providing intensive supportive care that do not compromise the safety of health workers are needed.

The issue of late deaths during the recovery phase is particularly disheartening to medical teams. It may also raise suspicion, fear and stigma against the Ebola Management Center and hamper acceptability by the community. Cardiac arrhythmias (as a result of severe electrolyte imbalances), myocarditis, pericardial effusions, encephalitis or other reasons may be to blame. Research into the cause of late mortality is important and should be pursued. There might also have been associated co-morbidity (eg HIV) that we were unaware of.

Finally, of serious concern is that 28 health workers were affected and suffered a higher casefatality than others. Surprisingly, health workers did not present earlier than the general population, which is worrying since symptomatic health workers are at high risk of both acquiring and transmitting infection. In a country that had only 0.2 doctors and 1.7 nurses per 10,000 inhabitants before the epidemic, additional staff losses are devastating and will have long-term repercussions for an already weak, crippled health system. Measures to improve health monitoring of staff are needed. On a wider scale, the number of infected health workers who died in West Africa from Ebola (592 infected and 340 deaths) shows that the medical community seems to have placed inadequate emphasis on safety and advocacy for health workers.

Focused immediate and long-term attention on a national scale is needed to ensure infection control and protection for the remaining health workers. Curbing the population spread of Ebola plus new vaccines and treatments would provide a safety net for health workers and need to be fast-tracked. Compensating for Ebola-related health worker attrition through accelerated training of new and adapted health worker cadres is urgently needed but dependent on international support.

# Conclusion

Despite severe limitations, commendable efforts have been made towards trying to control the Ebola outbreak in a rural district of Sierra Leone. The recovery rate of almost 50% in difficult circumstances is positive, but balanced by a significant loss of health care workers, woeful inadequacies of transport and case-

finding and difficult access to the Ebola Management Center. Urgent and sustained action by national and international partners is necessary to support Ebola Management Centers in all districts, solve operational problems and contain the epidemic.

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## REFERENCES

Baize S, Pannetier D, Oestereich L, *et al.* (2014) Emergence of Zaire Ebola virus disease in Guinea. New *England Journal of Medicine*, *371*, 1418-1425.

Bausch DG, Towner JS, Dowell SF, et al. (2007) Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. *Journal of Infectious Disease*, 196 Suppl 2, S142-147.

Bolten CE. (2014) Articulating the Invisible: Ebola Beyond Witchcraft in Sierra Leone http://www.culanth.org/fieldsights/596-articulating-the-invisible-ebola-beyond-witchcraft-insierra-leone.

Feldmann H & Geisbert TW. (2011) Ebola haemorrhagic fever. Lancet, 377, 849-862.

Fitzpatrick G, Vogt F, Moi Gbabai O, *et al.* (2014) Describing readmissions to an Ebola case management centre (CMC), Sierra Leone, 2014. *Euro Surveillance, 19*.

Gatherer D. (2014) The 2014 Ebola virus disease outbreak in West Africa. *Journal of General Virology, 95*, 1619-1624.

- Gostin LO, Lucey D & Phelan A. (2014) The Ebola epidemic: a global health emergency. *Journal of the American medical Association, 312,* 1095-1096.
- Khan AS, Tshioko FK, Heymann DL, *et al.* (1999) The reemergence of Ebola hemorrhagic fever, Democratic Republic of the Congo, 1995. Commission de Lutte contre les Epidemies a Kikwit. *Journal of Infectious Diseases, 179 Suppl 1*, S76-86.

Leroy EM, Kumulungui B, Pourrut X, et al. (2005) Fruit bats as reservoirs of Ebola virus. Nature, 438, 575-576.

MacNeil A & Rollin PE. (2012) Ebola and Marburg hemorrhagic fevers: neglected tropical diseases? *PLoS Neglected Tropical Diseases, 6*, e1546.

Meltzer MI, Atkins CY, Santibanez S, et al. (2014) Estimating the future number of cases in the ebola epidemic --- liberia and sierra leone, 2014--2015. MMWR Surveillance Summary, 63, 1-14.
Philips M & Markham A. (2014) Ebola: a failure of international collective action. Lancet, 384, 1181.

Piot P, Muyembe JJ & Edmunds WJ. (2014) Ebola in west Africa: from disease outbreak to humanitarian crisis. *Lancet Infectious Diseases*.

Schieffelin JS, Shaffer JG, Goba A, et al. (2014) Clinical Illness and Outcomes in Patients with Ebola in Sierra

Leone. New England Journal of Medicine.

Tomori O, Bertolli J, Rollin PE, *et al.* (1999) Serologic survey among hospital and health center workers during the Ebola hemorrhagic fever outbreak in Kikwit, Democratic Republic of the Congo, 1995. *Journal of Infectious Diseases, 179 Suppl 1*, S98-101.

- Ulrich CM. (2014) Ebola is causing moral distress among African healthcare workers. *British Medical Journal*, 349, g6672.
- Whitty CJ, Farrar J, Ferguson N, *et al.* (2014) Infectious disease: tough choices to reduce Ebola transmission. *Nature*, *515*, 192-194.

WHO (2014a) Ebola responce roadmap - Situation report. Available: http://www.who.int/csr/disease/ebola/situation-reports/en/?m=20141112 (Accessed 16th

November 2014)

WHO (2014b) Ebola virus disease in West Africa--the first 9 months of the epidemic and forward projections. New England Journal of Medicine, 371, 1481-1495.

WHO (2014c) Ebola Virus Disease. fact shet 103.

Available:http://www.who.int/mediacentre/factsheets/fs103/en/ (Accessed 11th November 2014) WHO (2014d) Ebola: vaccines therapies and diagnostics. Available:

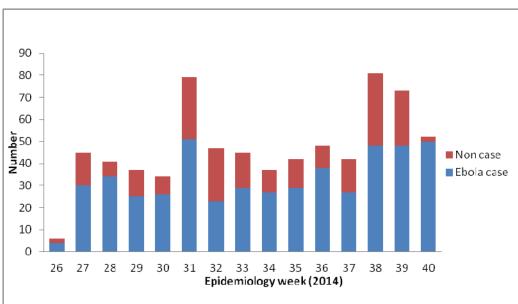
http://www.who.int/medicines/emp\_ebola\_section/en/ (Accessed 16th November 2014)

WHO (2014e) World Health Statistics.

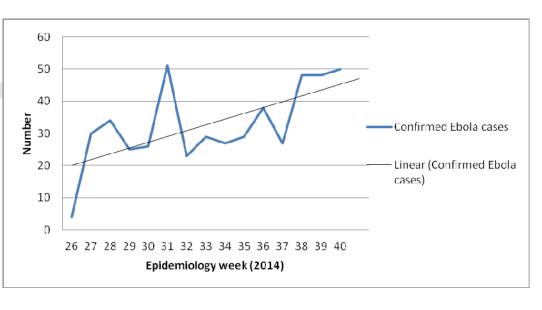
Available:http://www.who.int/gho/publications/world\_health\_statistics/2014/en/ (Accessed 11th November 2014)

**Corresponding author:** Rony Zachariah, Coordinator, operations research, Médecins Sans Frontières, Brussels operational centre, 6 Rue De Gasperich, Luxembourg. Phone + 352 661332516, Fax + 352 335133, email rony.zachariah@brussels.msf.org

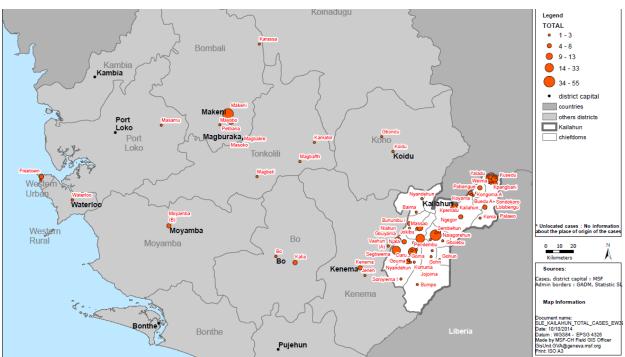
**Figure 1:** Trend in admissions to the Ebola Management Centre stratified by confirmed Ebola case and noncase, Kailahun, Sierra Leone during Epidemiology weeks 26-40 (June 23<sup>rd</sup> -October 5<sup>th</sup> 2014)



**Figure 2.**Trend in confirmed Ebola cases admitted to the Ebola Management Centre in Kailahun, Sierra Leone during Epidemiology weeks 26 to 40 (June 23<sup>rd</sup> -October 5<sup>th</sup> 2014)



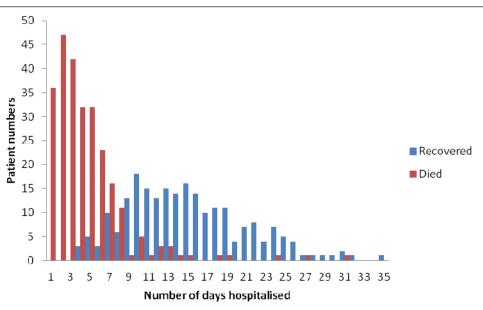
**Figure 3.** Mapping of confirmed Ebola cases admitted to the Ebola Management Centre in Kailahun, Sierra Leone during Epidemiology weeks 26-40 (June 23<sup>rd</sup>- October 5<sup>th</sup> 2014)



Area in white represents Kailahun district, Sierra Leone

Orange circles represent Ebola cases, the size of the circle being proportional to the number of cases

**Figure 4.** Length of hospitalization of confirmed Ebola cases among those who died or recovered at the Ebola Management Centre, Kailahun, Sierra Leone during Epidemiology weeks 26-40 (June 23<sup>rd</sup> –October 5<sup>th</sup> 2014)



**Figure 5:** Cumulative incidence of death among confirmed Ebola cases admitted to the Ebola Management Centre, Kailahun, Sierra Leone during Epidemiology weeks 26 to 40 (June 23<sup>rd</sup>-October 5<sup>th</sup> 2014)

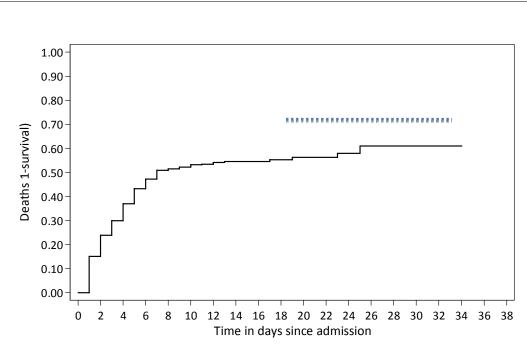


 Table 1: Clinical features at admission of confirmed Ebola cases recorded consecutively at the Ebola Management Centre, Kailahun, Sierra Leone (August –October 2014) \*

Clinical	features (n-245)	(%)
-	Fever	87%
-	Fatigue	77%
-	Headache	73%
-	Anorexia	72%
-	Joint pain	56%
-	Abdominal pain	51%
-	Diarrhoea	48%
-	Nausea/vomiting	46%
-	Chest pain	44%
-	Cough	40%
-	Difficulty swallowing	26%
-	Sore throat	26%
-	Difficulty breathing	20%
-	Hiccups	15%
-	Pain behind the eyes	12%
-	Confused/disoriented	9%
-	Jaundice	8%
-	Unexplained bleeding	5%
-	Skin rash	3%
-	Conjunctivitis	2%
-	Coma	1%

\* Clinical history was recorded consecutively only from August 2014 when such data collection was initiated in the project