Ebola Virus Disease in West Africa

The First 9 Months of the Epidemic and Forward Projections

Group 9

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Executive summary

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1 Introduction

In this report we will discuss the paper Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections. First we will elaborate on the background and the objective of the paper. After that, the methodologies used in the paper will be discussed, followed by an overview of the results. We will conclude with the contributions made by the paper and the limitations relating to the research of the paper.

1.1 Background & objective of the paper

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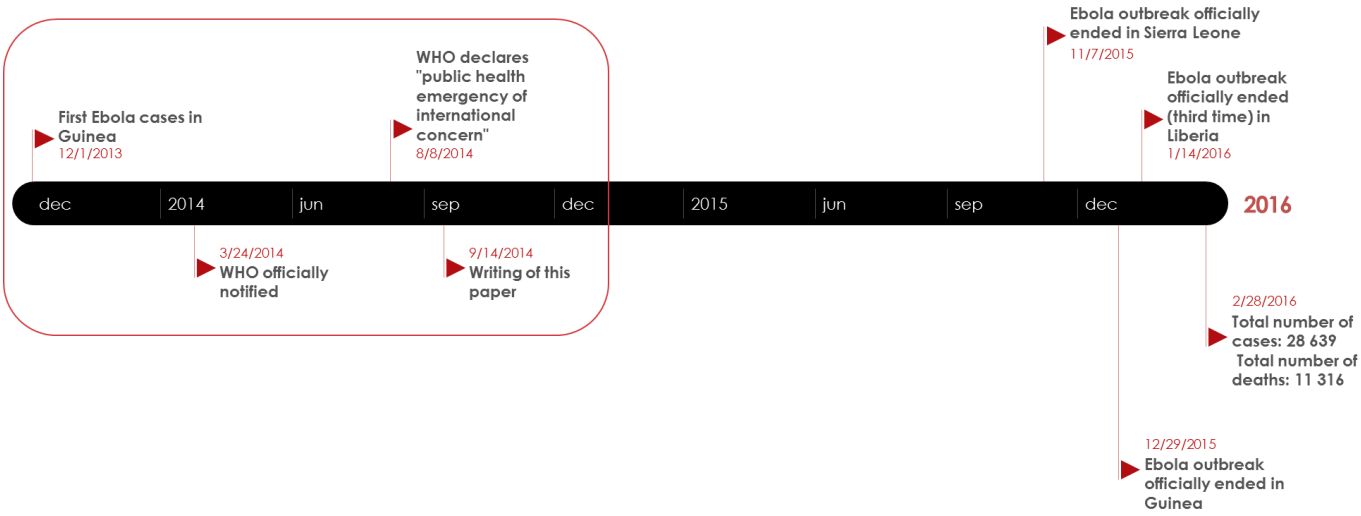
Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections written by the World Health Organisation (WHO) Ebola Response Team. Published on October 16th 2014 in the New England Journal of Medicine, Vol 371, No 16.

1. Explore the clinical and epidemiologic characteristics of the epidemic
2. Document trends in the epidemic
3. Project expected case numbers for the coming weeks if control measures are not enhanced.

Based on the first 9 months of the epidemic in Guinea, Liberia, Nigeria, and Sierra Leone



1.2 Issue the paper addresses

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- the sudden outbreak of Ebola
- At the moment of writing, #…. cases
- Signals that the disease will spread rapidly
- Urgency to do something

2 Methodology

To be able to reach the objectives of the paper, three different methods are used. First of all surveillance is used to collect sufficient data. The data is analysed by using Logistic Regression Modelling and the Reproduction Number R. Logistic Regression Modelling is used to explore the characteristics of the epidemic. The Reproduction number R will be the base for the projection of future cases.

2.1 Surveillance

Using a standard case investigation form the clinical and demographical data of patients were collected. In addition to this, these data were supplemented by information collected in informal case reports, data from diagnostic laboratories, and from burials. To create the fullest possible picture of the unfolding epidemic. The following aspects are included in the standard case investigation form:

- District of residence
- District of disease report
- Age
- Sex
- Signs and symptoms recorded
- Date of symptom onset
- Name of hospital
- Date of hospitalization
- Date of death or discharge

Some of the cases provided addition information about potentially infectious contacts with other EVD cases, including possible exposure at funerals.

According to the definition is the World Health Organisation, which is used in this paper, the cases are categorised in three categories:

- A suspected case
- A probable case
- A confirmed case

A suspected case *is illness in any person, alive or dead, who has (or had) sudden onset of high fever and had contact with a person with a suspected, probable, or confirmed Ebola case or with a dead or sick animal,* or *any person with sudden onset of high fever and at least three of the following symptoms: headache, vomiting, anorexia or loss of appetite, diarrhoea, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccupping,* or *any person who had unexplained bleeding or who died suddenly from an unexplained cause*. (SOURCE WHO)

A probable case is *illness in any person suspected to have EVD who was evaluated by a clinician or any person who died from suspected Ebola and had an epidemiologic link to a person with a confirmed case but was not tested and did not have laboratory confirmation of the disease*. (SOURCE WHO)

A case is classified as confirmed when *a sample of the patient tested positive for Ebola*. (SOURCE WHO)

The analysis is done based on the confirmed and probable cases, so the suspected cases are excluded. This results in an analysis on 3343 confirmed and 667 probable Ebola cases.

2.2 Logistic Regression Modelling

Using the cases with a definitive outcome (either the patient is death or recovered), logistic regression modelling is used to determine potential risk factors for a fatal outcome. The risk factors which are evaluated are:

- Sex
- Age group (< 15 years; 15 - 44 years; >44 years)
- Symptoms
- Occupation (healthcare worker; not healthcare worker)

For all symptoms the odds ratio was calculated, where only symptoms which had at least five observation were taken into account. Furthermore, the Case Fatality Rate (CFR) is calculated. The CFR is the percentage of fatal EVD cases among reported cases with a known definitive clinical outcome.

2.3 Reproduction Number R

The reproduction number R is the average number of secondary cases which arise, when a primary case is introduced into a population. When R is greater than 1, the disease can spread into the population. If R is smaller than 1, the number of cases will become smaller and smaller and the disease cannot sustain in the population. The calculation of R can be useful to get insights in the magnitude of the epidemic, the efforts which are required to control the virus, and to evaluate the effectiveness of control measures.

To calculate the reproduction number, the generation time is determined. The generation time is the time between infection in an index case patient and infection in a patient infected by that index case patient. Besides this, four other key time periods that characterise the spread of the virus are calculated:

- the incubation period, which is the time between infection and the onset of symptoms
- the interval from symptom onset to hospitalization
- the interval from hospital admission to death and the interval from hospital admission to discharge
- the serial interval, which is defined as the interval between disease onset in an index case patient and disease onset in a person infected by that index case patient

The initial value of R, called the basic reproduction number or R0, indicates how fast the virus will spread into the uninfected population. If the virus sustains the early phase, the number of cases will grow exponentially. Once the infection has become established within the population, the number of people still at risk declines. This results in a decline in the reproduction number R_o to a smaller number which is called net reproduction number, R_t.

Based on the data collected by surveillance, the two methods presented above will lead to the results presented in the next section.

3 Results of the data analysis

The results can be split into three parts: the scale and characteristics of the epidemic, the geographic origin and spread of the epidemic, and the projection of the number of future cases. This paragraph will elaborate on this three parts.

3.1 The scale and characteristics of the epidemic

The scale of the epidemic is made visual in different plots, where the weekly number of cases is plotted. One plot provides us with an overview of all the cases in the most affected countries, Sierra Leone, Nigeria, Liberia and Guinea (figure A). Figure B, C and D show the number of cases divided into the three categories suspected, probable and confirmed for Guinea, Liberia and Sierra Leone. As can be seen from the figures, the first cases started at the end of 2013 in Guinea. From July 2014 onwards there was a sharp increase in the number of cases in all three countries. Especially Liberia suffers from many cases.

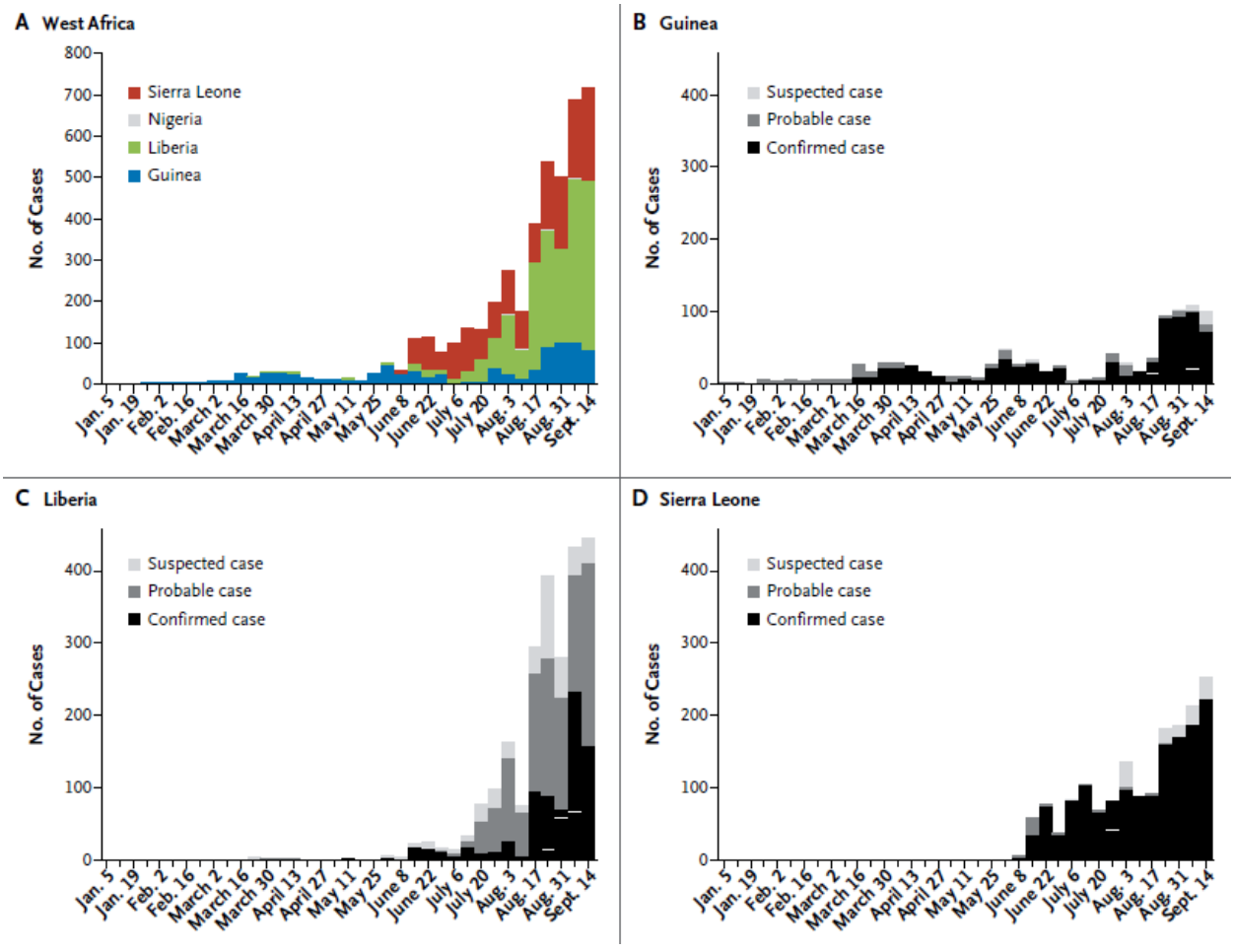

Figure 1: Weekly Incidence of Confirmed, Probable, and Suspected Ebola Virus Disease Cases

The demographic characteristics and most common symptoms of the epidemic are summarised in a table. There is no separation made into the different countries. The results can be found in table 1.

Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Demographic characteristics				
Male sex	685/1415 (48.4)	515/1056 (48.8)	170/359 (47.4)	0.93 (0.73–1.19)
Age group				
<15 yr	190/1378 (13.8)	145/1021 (14.2)	45/357 (12.6)	1.18 (0.83–1.71)
15–44 yr	838/1378 (60.8)	577/1021 (56.5)	261/357 (73.1)	0.48 (0.36–0.62)
≥45 yr	350/1378 (25.4)	299/1021 (29.3)	51/357 (14.3)	2.47 (1.79–3.46)
Health care worker	158/1429 (11.1)	112/1067 (10.5)	46/362 (12.7)	0.86 (0.60–1.27)
Signs and symptoms				
General symptoms				
Fever‡	1002/1151 (87.1)	746/846 (88.2)	256/305 (83.9)	1.34 (0.92–1.95)
Fatigue	866/1133 (76.4)	633/829 (76.4)	233/304 (76.6)	0.94 (0.68–1.28)
Loss of appetite	681/1055 (64.5)	498/778 (64.0)	183/277 (66.1)	0.92 (0.69–1.23)
Vomiting	753/1114 (67.6)	566/816 (69.4)	187/298 (62.8)	1.19 (0.89–1.59)
Diarrhea	721/1099 (65.6)	555/813 (68.3)	166/286 (58.0)	1.42 (1.06–1.89)
Headache	553/1035 (53.4)	407/757 (53.8)	146/278 (52.5)	1.03 (0.78–1.36)
Abdominal pain	439/992 (44.3)	311/715 (43.5)	128/277 (46.2)	0.85 (0.64–1.13)
Muscle pain	385/990 (38.9)	293/728 (40.2)	92/262 (35.1)	1.24 (0.92–1.67)
Joint pain	374/950 (39.4)	283/695 (40.7)	91/255 (35.7)	1.32 (0.98–1.80)
Chest pain	254/686 (37.0)	196/488 (40.2)	58/198 (29.3)	1.53 (1.07–2.20)
Cough	194/655 (29.6)	150/462 (32.5)	44/193 (22.8)	1.74 (1.18–2.61)
Difficulty breathing	155/665 (23.3)	123/472 (26.1)	32/193 (16.6)	1.68 (1.10–2.63)
Difficulty swallowing	169/514 (32.9)	138/375 (36.8)	31/139 (22.3)	2.22 (1.41–3.59)
Conjunctivitis	137/658 (20.8)	109/465 (23.4)	28/193 (14.5)	2.03 (1.29–3.29)
Sore throat	102/467 (21.8)	82/339 (24.2)	20/128 (15.6)	1.94 (1.13–3.46)
Confusion	84/631 (13.3)	68/446 (15.2)	16/185 (8.6)	2.00 (1.14–3.71)
Hiccups	108/947 (11.4)	91/699 (13.0)	17/248 (6.9)	2.15 (1.27–3.82)
Jaundice	65/627 (10.4)	52/443 (11.7)	13/184 (7.1)	1.83 (0.99–3.63)
Eye pain	48/622 (7.7)	39/438 (8.9)	9/184 (4.9)	1.95 (0.95–4.40)
Rash	37/642 (5.8)	30/453 (6.6)	7/189 (3.7)	1.90 (0.86–4.83)
Coma or unconsciousness	37/627 (5.9)	34/445 (7.6)	3/182 (1.6)	4.59 (1.61–19.34)
Unexplained bleeding	168/932 (18.0)	140/693 (20.2)	28/239 (11.7)	1.83 (1.20–2.90)
Hematemesis	26/670 (3.9)	20/503 (4.0)	6/167 (3.6)	1.07 (0.44–3.01)
Blood in stool	48/843 (5.7)	35/614 (5.7)	13/229 (5.7)	0.98 (0.52–1.96)
Bleeding gums	19/837 (2.3)	18/608 (3.0)	1/229 (0.4)	6.69 (1.35–121.32)
Bloody nose	16/836 (1.9)	15/610 (2.5)	1/226 (0.4)	8.02 (1.54–148.62)
Bloody cough	20/831 (2.4)	16/605 (2.6)	4/226 (1.8)	1.63 (0.58–5.82)
Other bleeding	8/657 (1.2)	5/493 (1.0)	3/164 (1.8)	0.45 (0.11–2.23)
Bleeding at injection site	20/833 (2.4)	19/605 (3.1)	1/228 (0.4)	6.51 (1.32–118.04)
Blood from vagina§	14/431 (3.2)	13/290 (4.5)	1/126 (0.8)	6.0 (1.11–112.4)
Blood in urine	10/827 (1.2)	9/601 (1.5)	1/226 (0.4)	5.14 (0.90–98.73)
Bleeding under skin	5/827 (0.6)	5/604 (0.8)	0/223	NA

Table 1: Demographic Characteristics and Signs and Symptoms in Confirmed and Probable Ebola Case Patients with a Definitive Clinical Outcome

The paper highlights that the case fatality rate is 70.8% (95%CI = 68.8 - 72.8). The median age of the patients is 32 years old. There were no significant differences in the median age between the different countries. Most patients are between 15 and 44 years old, 60.8%. Patients older than 44 have a higher chance to die from the Ebola virus, which can be concluded based on the odds ratio of 2.47 for this group of patients, which is a lot higher than for the other age categories. There is no significant difference in gender for the patients, so male and female have the same chance to get infected by the Ebola virus. Also for gender there is no significant difference between the different countries. The most common symptoms are Fever (87.1%), Fatigue (76.4%), Vomiting (67.6%), Diarrhoea (65.6%), Loss of Appetite (64.5%) and Headache (53.3%). For less common symptoms such as bloody nose and bleeding gums, the odds ratio is very high. More details can be found in table 1.

3.2 The geographic origin and spread of the epidemic

The first cases occurred in Guéckédou and Macenta districts in Guinea. During March 2014 the first cases were reported in Lofa and other districts in Liberia, and were followed by the discovery of cases in the capital of Guinea, Conakry. During May the epidemic in Guinea expanded to the neighbouring districts of Kenema and Kailahun in Sierra Leone. From July onwards there was a sharp increase in the number of cases in all three countries. Out of the 67 districts in the three countries, 43 reported Ebola cases. More than 90% of the cases has been reported in 14 of the districts. Figure 2 shows the geographic spread of the Ebola virus. Old cases are marked grey, where cases reported the last 21 days are marked red.

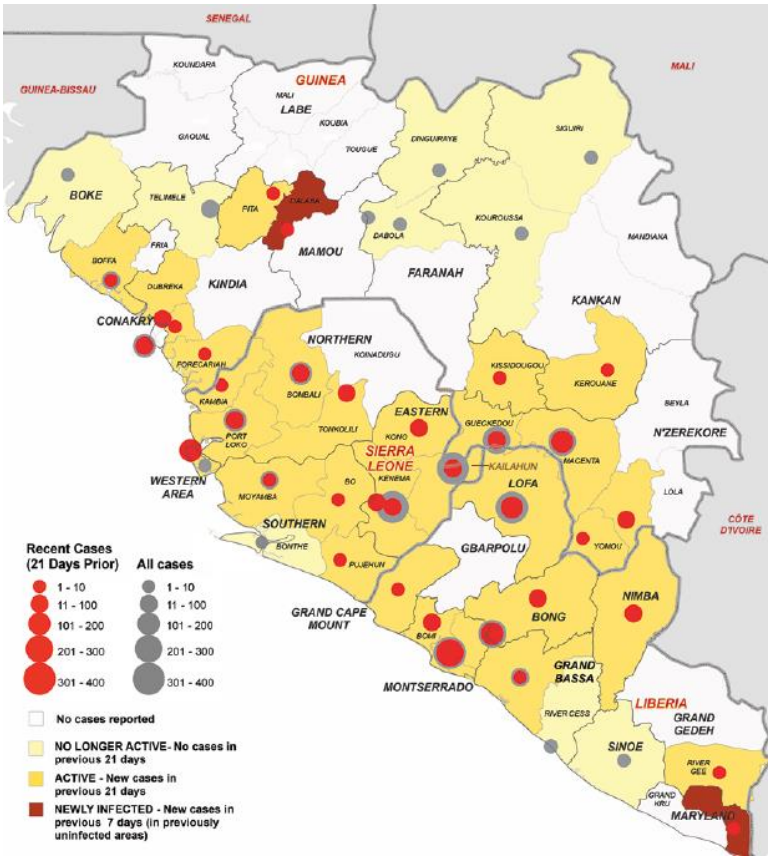

Figure 2: Districts Affected by Ebola Virus Disease

3.3 Projection of future cases

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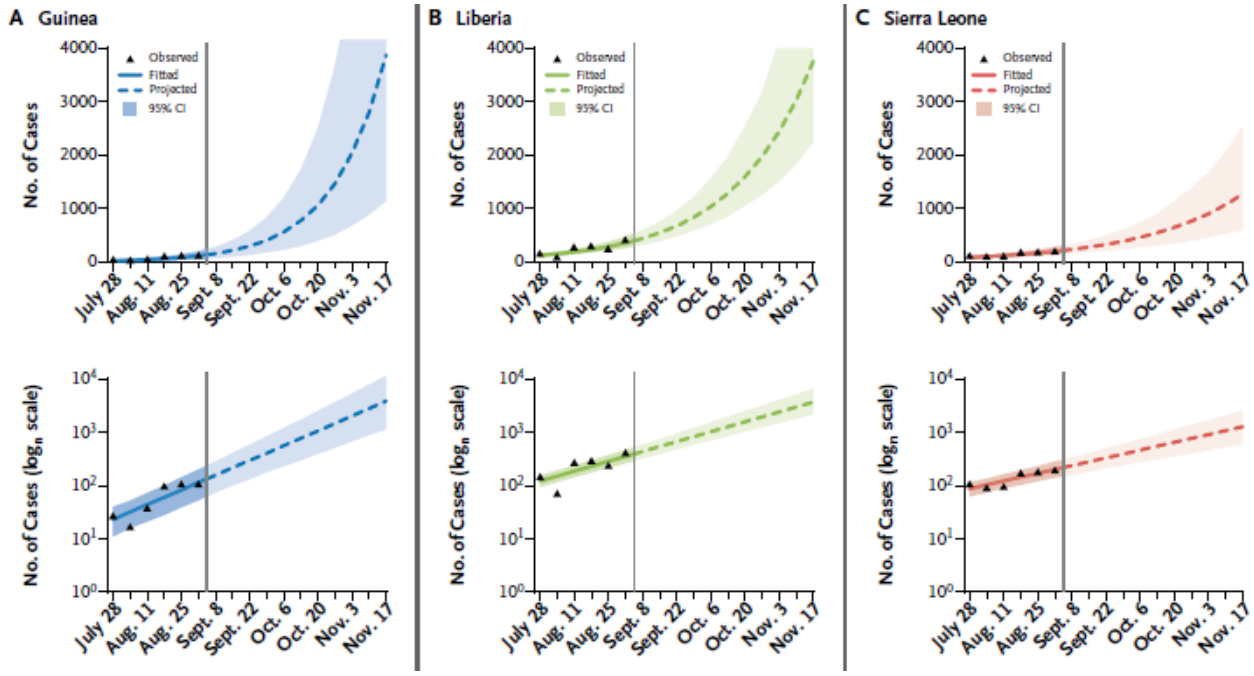

4 Conclusion

Based on the results of the analysis presented above, the authors of the paper conclude that the epidemic will keep expanding in the coming weeks if the control measures – improvements in contact tracing, adequate case isolation, increased capacity for clinical management, safe burials, greater community engagement, and support from international partners – do not change. The cumulative number of confirmed and probable cases will be 5740 in Guinea, 9890 in Liberia, and 5000 in Sierra Leone, exceeding 20,000 cases in total by the beginning of November.

The scale of this epidemic is exceptional large, even though the characteristics such as incubation period, the reproduction number and the most common symptoms are similar to those in previous Ebola outbreaks. Therefore the main cause of this large scale is not the virus itself, but rather the characteristics of the population and the (lack of) control measures. Due to the high interconnectedness between the population of Guinea, Liberia and Sierra Leone may have led to the rapid spread of the epidemic. However, Nigeria proved that a large outbreak can be avoided. The critical success factor seems to be the speed of the implementation of strict control measures.

4.1 Main contributions

The results from this paper provide us with several valuable insights regarding this deadly and large scale Ebola outbreak. First of all, it provides us with insights into the characteristics of the epidemic. By for example determining risk factors, groups who have a high risk of dying can be identified. Furthermore, insights into the most common symptoms and their odds ratio can make the treatment of patients more efficient, and can also indicate the need for medical supply. Based on the future projections, the need for hospital beds can be estimated. Since the current number of beds will probably be not sufficient, action is needed to increase the number of hospital beds. Besides this, the paper also provides insights into the spread of the epidemic, and in this way make it possible for control measures to be implemented more efficiently. Two control measures the paper suggests are to track Ebola cases for minimum 21 days and to lower the period from symptom onset to hospitalization.

Next to this valuable insights, the paper creates a general sense of urgency by showing how serious this Ebola outbreak is in number of patients and the fatality ratio. In this way a fast introduction of control measures, additional research to vaccines and help from international partners is stimulated.

4.2 Limitations

The conclusions drawn by this paper are based upon the collected data. This causes some limitations and interpretation of the data requires knowledge and care. It is certain that not all cases are reported or have been detected. The collected case records are often incomplete. This can lead to biased data, and can for example result in an underestimation of the future cases.

There are two main points of interest for future research, since this can be influenced by the incomplete case records. First, the serial interval of 15.3 days is longer than past estimations. This can be caused by the biased data, but if this serial interval turns out to be reliable the case isolation used so far has been less effective than expected. Second, the case fatality rate appears to be the same for all countries, based on the data with definitive outcomes. If all cases are taken into consideration,

differences between the countries become visible. Further research is necessary to create more certainty about this point.