We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

A Historical Review of Ebola Outbreaks

Kasangye Kangoy Aurelie, Mutangala Muloye Guy,
Ngoyi Fuamba Bona, Kaya Mulumbati Charles,
Avevor Patrick Mawupemor and Li Shixue

Additional information is available at the end of the chapter

Abstract

Ebola Virus Disease (EVD) is a severe, often fatal illness in humans caused by the Ebola virus. Since the first case was identified in 1976, there have been 36 documented outbreaks with the worst and most publicized recorded in 2014 which ravaged three West African Countries, Guinea, Liberia and Serial Leone. The West African outbreak recorded 28,616 human cases, 11,310 deaths (CFR: 57–59%) and left about 17,000 survivors, many of whom have to grapple with Post-Ebola syndrome. Historically, ZEBOV has the highest virulence. Providing a historical perspective which highlights key challenges and progress made toward detecting and responding to EVD is a key to charting a path towards stronger resilience against the disease. There have been remarkable shifts in diagnostics, at risk populations, impact on health systems and response approaches. The health sector continues to gain global experiences about EVD which has shaped preparedness, prevention, detection, diagnostics, response, and recovery strategies. This has brought about the need for stronger collaboration between international organizations and seemingly Ebola endemic countries in the areas of improving disease surveillance, strengthening health systems, development and establishment of early warning systems, improving the capacity of local laboratories and trainings for health workers.

Keywords: Ebola, outbreaks, world

1. Introduction

Ebola Virus Disease (EVD), formerly known as Ebola Hemorrhagic Fever (EHF) is a severe, often fatal illness in humans [1]. It has become well known and notified disease all over the world, since its last outbreak in Guinea, Sierra Leone and Liberia (December 2013). EVD is caused by the Ebola virus and is responsible for about 50–90% death in clinically diagnosed

cases [2]. Efforts to contain this disease have been the focus of the World Health Organization (WHO) and some other countries in recent times. Despite these efforts, no medicine has yet been licensed for the treatment of the disease [3]. The Ebola virus was first discovered in Zaire now called the Democratic Republic of Congo (DRC). The virus was named Ebola following the first outbreak in the town of Yambuku, which is near the Ebola River in DRC; it is at the hospital in this town that the first case of Ebola was identified in September 1976 by the Belgian doctor Peter Piot of the Institute of Tropical Medicine Anvers [4, 5]. This study aims to summarize old and new experiences of Ebola all over the world, in order to have an overview of all Ebola outbreaks and to propose strategies for better prevention and management of future outbreaks.

1.1. Etiology

The Ebola virus (EBOV) is the principal etiology of EVD [6], Ebola virus belongs to the family of Filoviridae, to the order of Mononegavirales which includes Rhabdoviridae and Paramyxoviridae. The virion is pleomorphic, producing "U"-shaped, "6"-shaped, or circular forms but the predominant forms of the virion most frequently seen by electron microscope are long tubular structures. It contains one molecule of linear, single-stranded, negative-sense RNA of 4.2×10^6 Da [7]. EVD is caused by five genetically distinct members of the Filoviridae family:

1. Zaire ebolavirus (ZEBOV): Up to 2000, Ebola virus (EBOV) was formerly designated by Zaire Ebola virus [8, 9]. And in 2002, to species Zaire ebolavirus [10, 11]. However, most scientific articles continued to refer to "Ebola virus" or used the terms Ebola virus and Zaire ebolavirus in parallel. Consequently, in 2010, a group of researchers recommended that the name "Ebola virus" be adopted for a subclassification within the species Zaire ebolavirus, with the corresponding abbreviation EBOV [12]. Previous abbreviations for the virus were EBOV-Z (for Ebola virus Zaire) and ZEBOV (for Zaire Ebola virus or Zaire ebolavirus). At present, ICTV does not officially recognize "Ebola virus" as a taxonomic rank, and rather continues to use and recommend only the species designation Zaire ebolavirus [13].

2. Sudan ebolavirus (SEBOV): Sudan virus was first introduced as a new "strain" of Ebola virus in 1977 [14]. Sudan virus was described as "Ebola haemorrhagic fever" in a 1978 WHO report describing the 1976 Sudan Ebola outbreak [15]. In 2000, it received the designation of Sudan Ebola virus [8, 9], and in 2002 the name was changed to Sudan ebolavirus [10, 11]. Previous abbreviations for the virus were EBOV-S (for Ebola virus Sudan) and most recently SEBOV (for Sudan Ebola virus or Sudan ebolavirus). The virus received its final designation in 2010, when it was renamed Sudan virus (SUDV) [12].

3. Côte d'Ivoire ebolavirus (CEBOV): The name Taï Forest ebolavirus is derived from Parc National de Taï (the name of a national park in Côte d'Ivoire, where Taï Forest virus was first discovered) and the taxonomic suffix ebolavirus (which denotes an ebolavirus species) [12]. Taï Forest virus was first introduced as a new "strain" of Ebola virus in 1995 [16]. In 2000, it received the designation Côte d'Ivoire Ebola virus [8, 9]. In 2002, the name was changed to Cote d'Ivoire ebolavirus [10, 11]. The virus received its final designation in 2010, when it was renamed Taï Forest virus (TAFV) [12].

4. Bundibugyo ebolavirus (BEBOV): Bundibugyo virus was first introduced as Bundibugyo ebolavirus in 2008 [16]. The name Bundibugyo virus is derived from Bundibugyo (the name of the chief town of the Ugandan Bundibugyo District, where it was first discovered) and the taxonomic suffix virus [12]. Another name introduced at the same time was Uganda ebolavirus [17]. Later publications also referred to the virus as a novel "strain" of Ebola virus [18], or as Bundibugyo Ebola virus [19]. The abbreviations BEBOV (for Bundibugyo ebolavirus) and UEBOV (for Uganda ebolavirus) [17], were briefly used before BDBV was established as the abbreviation for Bundibugyo virus [12].

5. Reston ebolavirus (REBOV): Reston virus was first introduced as a new "strain" of Ebola virus in 1990 [20]. In 2000, it received the designation Reston Ebola virus [26, 27], and in 2002 the name was changed to Reston ebolavirus [8, 9]. Previous abbreviations for the virus were EBOV-R (for Ebola virus Reston) and most recently REBOV (for Reston Ebola virus or Reston ebolavirus). The virus received its current designation in 2010, when it was renamed Reston virus (RESTV) [12].

1.2. Transmission

Transmission in most outbreaks, Ebola virus is introduced into human populations via the handling of infected animal carcasses. In these cases, the first source of transmission is an animal found dead or hunted in the forest, followed by person-to person transmission from index case to family members or health-care staff. Animal-to-human transmission occurs when people come into contact with tissues and bodily fluids of infected animals, especially with infected NHPs [21]. The most likely vector of the EBOV is the fruit bat, specifically *Hypsignathus monstrosus* (the hammer-headed fruit bat), *Epomops franqueti* (Franquet's epaulets fruit bat), and *Myonycteris torquata* (the little-collared bat) [22].

Between 1976 and 1998, in 30,000 mammals, birds, reptiles, amphibians and arthropods sampled from regions of EBOV outbreaks, no Ebola virus was detected apart from some genetic traces found in six rodents (belonging to the species *Mus setulosus* and *Praomys*) and one shrew (*Sylvisorex ollula*) collected from the Central African Republic [23, 24]. Further research efforts have not confirmed rodents as a reservoir [25]. Traces of EBOV were detected in the carcasses of gorillas and chimpanzees during outbreaks in 2001 and 2003, which later became the source of human infections. The high rates of death in these species resulting from EBOV infection make it unlikely that these species represent a natural reservoir for the virus [23]. Antibodies against Zaire and Reston viruses have been found in fruit bats in Bangladesh, suggesting that these bats are also potential hosts of the virus and that the filoviruses are present in Asia [26].

The means of transmission within bat populations remain unknown [27]. Human disease is thought to result from consumption of poorly-cooked infected animals, such as bats or chimpanzees (which are known to feed on bats) [22, 28]. According to the findings of the WHO in October 2014, the most infectious fluids are blood, feces and vomit. The virus has also been detected in breast milk and urine [29]. However unlike other zoonosis, Ebola has the potential of spreading from human to human through exposure of mucous membranes or broken skin to infected body fluids including large aerosol droplets that can be produced during coughing [30].

1.3. The clinical features

The clinical features can be divided into four main phases as follows:

(Phase A) Influenza–like syndrome: The onset is abrupt with non-specific symptoms or signs such as high fever, headache, arthralgia, myalgia, sore throat, and malaise with nausea.

(Phase B) Acute (day 1–6): Persistent fever not responding to antimalarial drugs or to antibiotics, headache, and intense fatigue, followed by diarrhea and abdominal pain, anorexia and vomiting.

(Phase C) Pseudo-remission (day 7–8): During this phase the patient feels better and seeks food. The health situation presents with some improvement. Some patients may recover during this phase and survive from the disease.

(Phase D) Aggravation (day 9): respiratory disorders (dyspnea, throat and chest pain, cough, hiccups), symptoms of hemorrhagic diathesis (bloody diarrhea, hematemesis, conjunctival injection, gingival bleeding, nosebleeds and bleeding at the site of injection consistent with disseminated intravascular coagulation), skin manifestations (petechiae, purpura, morbilliform skin rash), neuropsychiatric manifestations (prostration, delirium, confusion, coma) and cardio-vascular distress and hypovolemic shock (death) [7].

Patients do not transmit Ebola during the incubation period but become infectious once they develop clinical features of EVD [30]. From the clinical manifestations it is obvious that EVD may mimic many other tropical diseases like malaria, typhoid fever or yellow fever at the start of the disease. In most outbreaks, recognition of the disease is delayed because physicians are not accustomed to this new illness and the symptoms are generally non-specific. Outside the epidemic context, it appears quite impossible to recognize the first Ebola case in an outbreak on clinical grounds only. Suspicion of EVD is only possible later during the aggravation phase [7].

2. Methodology

This study aims to summarize results of publications on all Ebola outbreaks. In order to accomplish this work, information was taken from databases such as PubMed and Cochrane library, and some articles were also taken from Google Scholar. This search will focus on past and present Ebola outbreaks all over the world. For some abstracts that met the predefined inclusion criteria, full texts were obtained. The data collection was focused more on some aspects of each outbreak such as: the year of the outbreak, the geographical spread (estimated area covered by the outbreak, country and region), and the strain of the virus involved in each outbreak, the index case, the case fatality, the diagnosis and the treatment used to control the situation. All the data will be put in Microsoft Excel software for construction of graphs. The data collection started on first July and ended on first August 2017; and a total of 23 full text and 6 abstracts were selected for the data extraction.

3. Ebola outbreaks characteristics (1976–2017)

This section will focuses on the characteristics of all Ebola outbreaks. In total, there have been 36 documented Ebola outbreaks that can be grouped into two: Major/Massive cases and Minor/Single cases.

3.1. Major outbreaks

Major outbreaks are larger outbreaks with more than 10 human registered cases of EVD (19 outbreaks).

The table highlights each major outbreak, the viral species responsible for the outbreak with the specie that induce the EVD, the country and the year in which the outbreak occurred, and the number of cases and deaths recorded. **Table 1** shows also after the West African Ebola Epidemic, Uganda is the second country in terms of number of cases, it has registered a lot of cases of Ebola during its first outbreak of 2000–2001 (425 cases/224 deaths).

3.2. Minor outbreaks

Minor/Single cases: these are smaller outbreaks with less than 10 human cases of EVD (17 outbreaks in total) (**Table 2**: minor Ebola outbreaks).

The DRC (Zaire) has recorded the highest number of EVD outbreaks (8 in total). It is also important to note that some of the Ebola cases were asymptomatic in minor outbreak such as in the Philippines 1, Philippines 3 and USA 2 outbreaks.

3.3. Case fatality rate of Ebolavirus

A case fatality rate (CFR) or case fatality risk is a property of an infectious disease in a particular population which states the risk of fatality due to the disease per case [31].

Figure 1 shows the distribution of case fatality by outbreaks (major outbreaks).

Figure 1 shows that the highest case fatality of major EVD outbreak in the all story of Ebola was recorded in the first outbreak in the Republic of Congo caused by ZEBOV (90%). and the lowest case fatality occurred in the fourth Ugandan outbreak caused by SUDV (34%). This corroborated with Literature that has reported Zaire species to have a higher case fatality than Sudan and Bundibugyo species, case fatality rates for ZEBOV as high as 90% [32].

3.4. Distribution of outbreaks by species of Ebola virus

Figure 2 shows how often each species of Ebola virus has been observed in the registered outbreaks. **Figure 2** also shows that ZEBOV is most commonly reported specie responsible for Ebola outbreaks.

Name*	Year	Cases/deaths	Country (city)/strain
Zaire1	August 1976	318/280	Zaire (Democratic Republic of Congo/DRC) in Yambuku/ZEBOV
Sudan1	November 1976	284/151	Sudan occurred in Nzara, Maridi, Tumbura and Juba/SUDV
Sudan2	1979	34/22	Sudan occurred in Nzara and Maridi/SUDV
Gabon1	1994	52/31	Gabon occurred in Makokou/ZEBOV
Zaire3	1995	315/254	Zaire in Kikwit/ZEBOV
Gabon2	1996 (January to April)	37/21	Gabon in Mayibout area/ZEBOV
Gabon3	1996–1997 (July to January)	60/45	Gabon occurred in Booue area/ZEBOV
Uganda1	2000–2001	425/224	Uganda in the Gulu, Masindi, and Mbarara district/SUDV
Gabon4	2001–2002 (October to July)	135/107	Gabon and Republic of the Congo/ZEBOV
Congo1	2002–2003(December to April)	143/128	Republic of Congo in the district of Mbomo and Kelle/ZEBOV
Congo2	2003 (November to December)	35/29	Republic of Congo occurred in Mbomo and Mbandza/ZEBOV
Sudan3	2004	17/7	Sudan in Yambio/SUDV
DRC1	2007	264/187	DRC in Kasai-Occidental province/ZEBOV
Uganda2	2007–2008 (December to January)	149/47	Uganda in the Bundibugyo district/BDBV
DRC2	2008–2009 (December to Febuary)	32/14	DRC occurred in Mweka and Luebo/ZEBOV
Uganda4	2012 (June to August)	24/17	Uganda in Kibaale district/SUDV
DRC3	2012 (June to November)	77/36	DRC in the Orientale Province/BDBV
West Africa	2013–2016	28.161/11,310	West African Ebola Virus Epidemic:
			Liberia, Sierra Leone, Guinea
			It began in Gueckedou (Guinea) in December 2013
			ZEBOV
DRC4	2014 (August to October)	66/49	DRC in the Equateur Province/ZEBOV

Notes: Sudan here refers to South Sudan, formerly Sudan.

*Chronological Name of outbreak with the country name as the prefix and the number of time that outbreak occurred in that country as the suffix.

Table 1. Major Ebola outbreaks.

3.5. The West African outbreak (December 2013–2016)

The West African EVD outbreak still and remains the most severe and largest outbreak. It has divested 3 principal countries: Liberia, Sierra Leone and Guinea, and spread abroad. Small outbreaks occurred in Nigeria and Mali [33, 34], and isolated cases were recorded in Senegal [35],

Name[*]	Year	Number of reported cases/number of death	Country (city)/strain
UK1	1976	1 case/0 death	United Kingdom/ZEBOV or SUDV
Zaire2	1977	1 case/1 death	Zaire in Tandala/ZEBOV
Philippines1	1989–1990	3 cases (asymptomatic)/0 death	Philippines/RESTV
USA1	1989	0 case/0 death	United States/RESTV
USA2	1990	4 cases (asymptomatic)/0 death	United States/RESTV
Italy1	1992	0 case/0 death	Italy/RESTV
C.I 1	1994	1 case/0 death	Cote d' Ivoire in Tai National Park/TAFV
C.I 2	1995	1 case/0 death	Cote d' Ivoire
SAF1	1996	2 cases/1 death	South Africa/ZEBOV
USA3	1996	0 case/0 death	United States/RESTV
Philippines2	1996	0 case/0 death	Philippines/RESTV
Russia1	1996	1 case/1 death	Russia/ZEBOV
Phillippines3	2008	6 cases (asymptomatic)/0 death	Philippines/RESTV
Uganda3	2011	1 case/1 death	Uganda in Luwero district/SUDV
Uganda5	2012–2013	6 cases/3 death	Uganda in Luwero district/SUDV
Phillipines4	2015	0 case/0 death	Philippines/RESTV
DRC5	2017	8 cases/4 death	DRC/ZEBOV

[*]Chronological Name of outbreak with the country name as the prefix and the number of time that outbreak occurred in that country as the suffix (e.g., Uganda 3 means the third outbreak in Uganda).

Notes: RESTV usually cause EVD in primates and others animals such as pigs, that why some of the outbreaks with RESTV as specie had 0 human cases and 0 deaths means that it was found in animals and not in human. However, Human being can get EVD with RESTV and not developed symptoms (that is the case of asymptomatic human cases of EVD).

Table 2. Minor Ebola outbreaks.

the United Kingdom and Sardinia [36, 37]. In addition, imported cases led to secondary infection of medical workers in the United States and Spain but did not spread further [38, 39].

Figure 3 shows the location of the West African Ebola outbreak.

It began in Guéckédou (Guinea) in December 2013 [41], On 25 March 2014 the WHO indicated that Guinea's Ministry of Health had reported an outbreak of Ebola virus disease in four southeastern districts, and that suspected cases in the neighboring countries of Liberia and Sierra Leone were being investigated [42], and on 29 March 2016, the WHO terminated the Public Health Emergency of International Concern status of the outbreak [43–45]. 28,616 human reported cases and 11,310 human deaths were registered with a case fatality of 57–59% (Among hospitalized patients [46, 47]. The outbreak left about 17,000 survivors of the disease, many of whom report post-recovery symptoms termed post-Ebola syndrome, often severe enough to require medical care for months or even years [48].
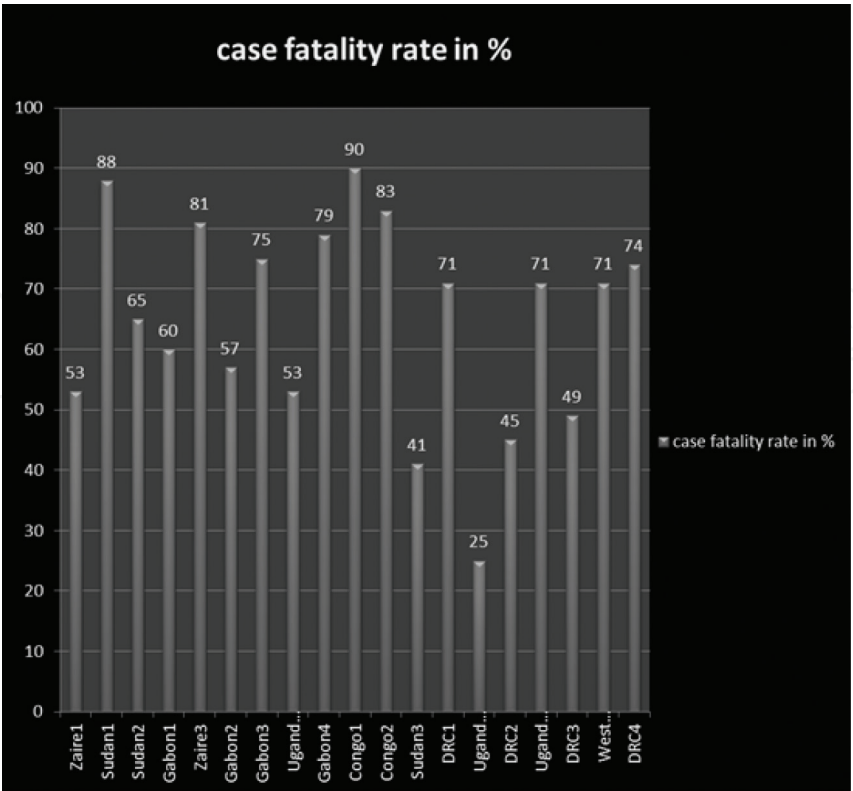
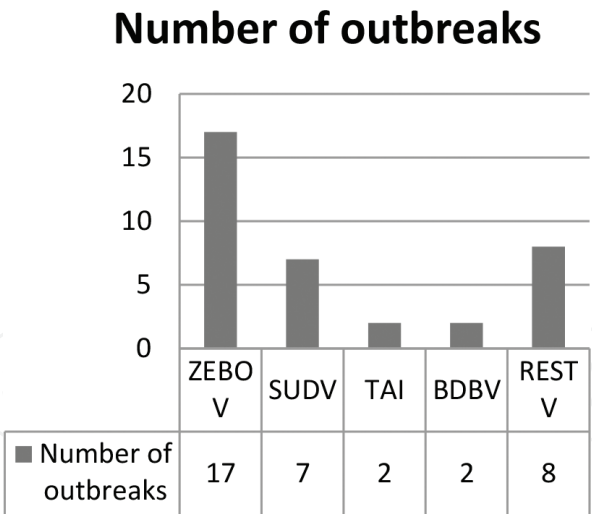**Figure 1.** Distribution of case fatality rate by major outbreaks.

Figure 2. Distribution of outbreaks by species of Ebola virus.

Table 3 shows that Liberia registered a high number of Ebola cases as the number of deaths in the West African outbreak, however the high case fatality (in major outbreaks) was reported in Guinea.

It is worth noting that Nigeria was the first West African country to be declared Ebola free (20 October 2014) [49].
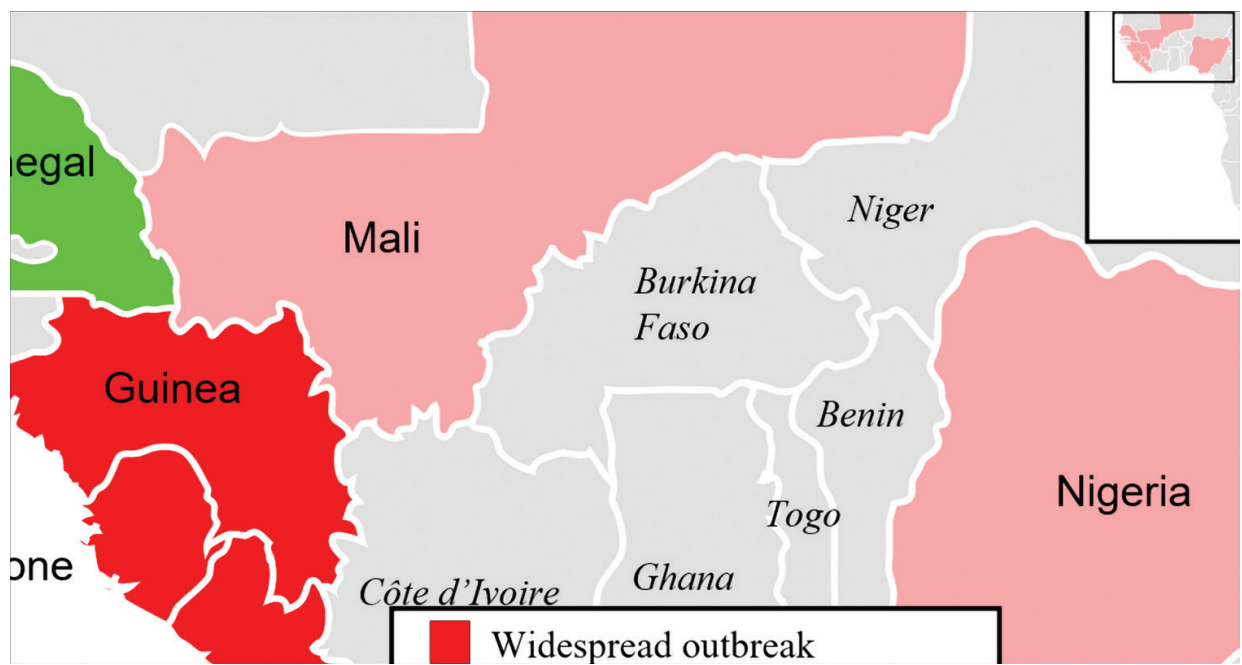
Figure 3. West African Virus Epidemic map [40].

Country	Number of cases	Number of deaths	Case fatality
Liberia[*]	10,666	4806	45%
Sierra Leone[*]	14,122	3955	28%
Guinea[*]	3804	2536	66%
Nigeria	20	8	40%
Mali	8	6	75%
USA	4	1	25%
Italy	1	0	0
UK	1	0	0
Senegal	1	0	0
Spain	1	0	0
Total	28,616	11,310	

[*]Major West African outbreak (Guinea, Liberia and Sierra Leone).

Table 3. Distribution of reported cases by countries in West African Ebola Epidemic.

3.6. Index cases

The index case, primary case, or patient zero is the initial patient in the population of an epidemiological investigation [50, 51]. The index case may indicate the source of the disease, the possible spread, and which reservoir holds the disease in between outbreaks. The index case

is the first patient that indicates the existence of an outbreak. Earlier cases may be found and are labeled primary, secondary, tertiary, etc. [52].

In most of EVD outbreaks the index cases have to be in contact of a virus reservoir, eat an animal found dead or hunted in the forest, or also a traveler who was in contact with an Ebola case (Medical professionals for example). The index case of EVD is the point on which the human to human transmission starts; he is the bridge between animal and human transmission of the disease.

A Chronological list of some index cases in the history of Ebola:

1. The first recorded victim of the Ebola virus was a 44-year-old schoolteacher named Mabalo Lokela (in Zaire/DRC), who felt ill after eating fresh and smoked antelope and monkey; he died on 8 September 1976 [53].

2. In 1994 (Cote d' Ivoire) a scientist became ill after conducting an autopsy on a wild chimpanzee in the Tai Forest. The patient was treated in Switzerland [16].

3. In 1995 (Zaire) the index case was farming and preparing charcoal in the remnant forest areas of Kikwit, there were a lot of bats and rodents in the region [54].

4. In 1996 (January-April) in Mayibout area (Gabon), a chimpanzee found dead in the forest was eaten by people hunting for food. Nineteen people who were involved in the butchery of the animal became ill [55].

5. In 1996 (South Africa) a medical professional traveled from Gabon to Johannesburg, after having treated Ebola-infected patients and having been exposed to the virus. He was hospitalized, and a nurse who took care of him became infected and died [56].

6. 1996–1997 (Gabon) Occurred in Booué area with transport of patients to Libreville. Index case-patient was a hunter who lived in a forest camp. Disease was spread by close contact with infected persons. A dead chimpanzee found in the forest at the time was determined to be infected [55].

7. In 2000–2001 (Uganda): a farmer in Rwot Obillo village, 14 kilometers North of Gulu town was the index case [57].

8. In 2007 (DRC/Zaire) In Mweka, Kasai Occidental Province. The index case was the chief of the village and a hunter [58].

9. In 2011 (Uganda): On the 5th of May, a 13-year-old girl was admitted to Bombo hospital, the Sudan Ebola subtype was detected and confirmed [59].

10. In 2012 (Uganda): The index case was a 16-year-old female from a remote rural community. She fell sick while preparing forest land with her husband for the planting season. Nine relatives who participated at the funeral died including a mother, and several sisters who contracted the infection died [59].

11. In 2013 (West African outbreak), 2-year-old Emile Ouamouno is believed to be the index patient in the 2014 Ebola epidemic in Guinea and West Africa [60]. Scientists have long believed that bats are involved in the spread of the virus, and, incidentally, the boy's home

was in the vicinity of a large colony of Angolan free-tailed bats. The Ebola virus was, however, not found in any of the bats that were captured and tested [61]. His mother, sister, and grandmother later became ill with similar symptoms and also died; people infected by these initial cases spread the disease to other villages [62, 63].

12. In 2014 (DRC/Zaire) in the Equator province, the index patient was a pregnant woman living in Inkanamongo village, who butchered a monkey [64].

13. 2017 (DRC/Zaire), the first patient to be seen was a 39-year-old man who reported to the local health facility on 22nd April 2017. He was immediately referred to Likati health zone facility but he died in transit. On 24th April 2017, a motorcycle rider (who transported the first patient) and another person who supported the first patient during transportation developed acute febrile illness. The motor cycle rider subsequently died on 26 April 2017. Other people who were close to these patients eventually developed similar illness [65].

3.7. Ebola virus in health care workers

Morbidity and mortality caused by EVD among health care workers has been very important. The major difference between the management of the Ebola epidemic and others, such as the HIV epidemic, is that the Ebola virus presents a more challenging health hazard to health care providers. Nurses, doctors, Red Cross volunteers, and other health care workers stand the risk of being infected with the Ebola virus while providing care. The risk of EVD contamination among these health care workers is also increased in a continent like Africa where the nurses and other health care providers work under extraordinarily difficult conditions, lacking such basic infection control tools as bleach, soap, and gloves [2]. When an Ebola patient, comes with non-diagnosed EVD in a hospital, the chain of contamination can start with the health care provider that offers the first care [3].

The first and famous example of a contaminated health worker is the nurse Mayinga N'Seka, who died in the 1976 outbreak in Zaire (now DRC) and to whom the prototype Ebola virus variant Mayinga (EBOV/May) was named [66]. The 1995 Democratic Republic of the Congo (DRC) outbreak devastated health care workers, out of the 250 individuals who died, 47 (approximately 20%) were health care professionals [58]. In Uganda, in the first outbreak of 2000–2001, the were 31 health workers among victims; And in the 2007 outbreak, 14 health care workers were among the victims [59]. Another example is the case of a Congolese (DRC) doctor and three health workers, who undertook a postmortem cesarean section on the index case of the 2014 outbreak. Both were not only infected and died; but became the evident source of further transmission in this outbreak. And from that outbreak, there were 49 registered deaths, of which 8 were health care professionals [64].

In the West African outbreak, it was estimated that, depending on their occupation in the health service, health workers were between 21 and 32 times more likely to be infected with Ebola than people in the general adult population. WHO estimated that large number of nurses and nurse aides have been affected, accounting for more than 50% of all health worker infections with occupation reported. Other categories of health workers affected include medical workers (doctors and medical students (12%), laboratory workers and trade and elementary workers (janitors, maintenance staff, etc.) with 7% each [67]. In a study done only in

Guinea in 2015, among Guinean health care workers, incidence of Ebola infection was highest among laboratory technicians (34.7 per 1000) and doctors (26.6 per 1000), followed by midwives (8.7 per 1000) and nurses (5.5 per 1000) [68].

Many other health care workers have been contaminated while taking care of EVD patients in Africa and imported to other continents, thereby becoming the index cases for those countries. Examples are the United Kingdom (Glasgow, 2014), where a nurse coming from Sierra Leonne was considering a first case of Ebola to be diagnosed on British soil [69] and in USA (Texas, 2014), a healthcare worker coming from Liberia, reportedly a female nurse at Texas Presbyterian Hospital was the first known person-to-person transmission case of Ebola in the US [70].

In Africa, especially in rural area, Ebola outbreaks have been linked to many rumors and legends. The existence of rumors and legends related to the outbreaks could obscure the viral nature of the disease [7], and this can lead to difficulty, for health workers, to easily accomplish their tasks. Nurses and doctors had to deal with not only a panicked and fearful public, essentially absent public health and medical resources, but also they themselves were seen as agents of death [2]. In Kikwit (DRC), anyone associated with Ebola was likely to have experienced stigmatization. At a point during the outbreak, local people thought Ebola originated from the medical staff working in the hospital. All those who had died had been in a hospital. Therefore, the people reasoned that, it was the health care workers who were killing the people [2]. In West African countries some patients were taken to traditional healers rather than science in a bid to combat the disease [71, 72]; increasing then the risk of contamination in the population.

3.7.1. Example of the experience of a health worker in Ebola outbreaks

Doctor Bona Ngoyi one of the co-authors, who has provided health care to EVD patientS in three outbreaks: firstly in the 2014 outbreak in DRC, secondly in the West African outbreak in Guinea (2015) and thirdly in the last outbreak (2017) in the DRC- reported that: "*the general objective of the mission was to provide technical support in the fight against Ebola in all outbreaks. But each outbreak faces different challenges. For example, when i was assigned to the prefecture of Dubréka in Guinea (11 March 2015 to 10 May 2015). The big challenge in this area was the management of EVD cases alerts; the active management of EVD was facing a lot of challenges such as: lack of good health care structures without standardized checklists of the cases, inadequate collaboration of certain families which hinder proper contact tracing activities. Thus, there were confirmed cases whose source cases were unknown. The mobility of cases was also a major challenge in managing this particular epidemic in Dubreka, patients with EVD could travel from a village to another, spreading the disease. It should be pointed out that our mission in Dubreka prefecture was characterized by lack of enthusiasm. Several times, the teams of supervisors, care teams and the Red Cross were assaulted by the villagers, making the task very difficult to all health workers.*"

Talking about Ebola outbreaks in the DRC, he also reported that: "*The management of Ebola in the DRC seems to be simplified by the facts that the population were a little informed about the disease, and rumors and legends seemed to disappear with time, because DRC has registered a high number of Ebola outbreaks and people are accepting to collaborate with health workers. The big challenges however have to do access the region concerned by the outbreak. These areas are often located in the Huge Equatorial Forest, which doesn't have good roads and Health structures*" (**Figures 4** and **5**).

Figure 4. Dr. Bona Ngoyi explaining hand washing techniques to the population of Boende (Equator province) during the 2014 Ebola outbreak in DRC.

Figure 5. Dr. Bona Ngoyi and his colleague using a boat to Likati (Equator province in DRC) to provide health care to the population during 2017 Ebola outbreak.

3.8. Treatment

There is no effective drug for EVD. Only supportive care could be administered, to sustain cardiac and renal functions with prudent use of perfusion. Oral rehydration can be recommended but sometimes not realistic because of throat pain, vomiting and intense fatigue [7].

In a clinical experiment conducted late in the 1995 Ebola outbreak in Kikwit, human convalescent blood was used for passive immunization to treat patients that had been infected naturally with ZEBOV; seven out of eight patients, who received blood transfusion from convalescent Ebola patients survived [72]. Such experiments, unfortunately, have not been repeated in further outbreaks because in vitro studies showed that antibodies against Ebola had no neutralizing activities. In addition, although monoclonal antibodies to the glycoprotein of Ebola virus showed protective and therapeutic properties in mice, they failed to protect NHP [73, 74]. Four laboratory workers in Russia who had possible Ebola exposure were treated with a combination of a goat-derived anti-Ebola immunoglobulin plus recombinant

human interferon alfa-2. One of these patients had a high-risk exposure and developed clinical evidence of Ebola virus infection. All 4 patients recovered [75].

Many others Ebola vaccine candidates had been developed in the decade prior to 2014 [76]. In December 2016, Ebola virus disease was found to be 70–100% prevented by rVSV-ZEBOV vaccine, making it the first proven vaccine against the disease [77, 78].

4. Evolution of Ebola disease overtime

This section will focuses on key historical developments of Ebola disease over time.

4.1. Geographical evolution of the disease (country or regional spread)

For More than 3 decades (1976–2013), all major Ebola outbreaks were occurred in Central African countries: DRC, Uganda, Sudan, Congo, and Gabon. This could be linked to the Equatorial forest which covers all these countries: It has been shown that tropical rain forests of Africa to which the Western Congo Swamp Forests near Yambuku and Minkebé Forest in Gabon belong constitute a common ecosystem for Ebola virus emergence providing rich animal biodiversity and as such epidemics appear to be seasonal. Documented human and non-human EVD outbreaks occurred mainly during wet seasons, marked by fruit abundance. The index case of the 1995 EVD outbreak in Kikwit fell ill in January and the 1994 EVD outbreak among chimpanzees in the Tai forest occurred in November, at the end of the wet season [7]. It is also interesting to note that the center of outbreaks has always been in areas bordering on forests (ecotone forest-savannah in the Democratic Republic of Congo, savannah in Sudan) [79]. In Uganda, the regions (Luwero, Kibaale, Gulu) in which the outbreak occurs are areas bordering forests. The equatorial forest is a poorly developed region, where the population lives essentially by hunting [3]; this can increases contact with animals or animal's carcasses which could be potential reservoir of the virus.

Ebola outbreaks tend to occur more in a rural areas than urban areas, while the West Africa outbreak marks the first outbreak in a densely populated urban area within Conakry's large shanty towns [80]. Ebola outbreak has changed in its region of occurrence from central Africa to western African countries in 2013, and spread (isolated cases) all over the world (USA, UK, Italy). It is important to note that the index case in most of the outbreak comes from the rural area.

4.2. Severity evolution of the Ebola strain

Studies have shown that the high case-fatality rate for Ebola virus is attributed to Zaire Ebola virus species (50–90%), the case fatality for SUDV range from 40 to 60% [81, 82] and approximately 40% for BDBV [19]. Only one person has been infected with the Taï Forest strain and survived the illness [82, 83]. RESTV specie seems to be less pathogenic to humans. In a meta-analysis of WHO data from 20 outbreaks involving Zaire, Sudan and Bundibugyo Ebola species, including the 2014 West African outbreak, the average case fatality rate was estimated to be 65.4%, and ZEBOV case fatality was reported to decrease with time [84]. It is important to note that the more the country registered the outbreak, more the case fatality decrease: this

could be explained by the fact that the health workers of a region which has registered several Ebola outbreaks will be trained to contain the disease than those in other regions which have never experienced the disease.

Another factor that could increase the severity of Ebola in Africa could be the co-infection of Ebola and Malaria or with other tropical diseases. The researchers found that malaria co-infection; extremes in age and delayed healthcare seeking behavior were all associated with mortality. Additionally, symptoms including disorientation, hiccups, diarrhea, and conjunctivitis, shortness of breath and muscle aches were all predictors of death in a very short time [85].

4.3. Changes and progress in diagnostic techniques for Ebola

Laboratory diagnosis of Ebola virus disease plays a critical role in outbreak response efforts; however, establishing safe and expeditious testing strategies for this high-biosafety-level pathogen in resource-poor environments remains extremely challenging. Since the discovery of Ebola virus in 1976 via traditional viral culture techniques and electron microscopy, diagnostic methodologies have trended towards faster, more accurate molecular assays. Importantly, technological advances have been paired with increasing efforts to support decentralized diagnostic testing capacity that can be deployed at or near the point of patient care [86]. Since the West African outbreak, efforts have been done to find a rapid and safe test for diagnosis of Ebola.

Diagnosis of Ebola has changed from cell culture, Antibody detection, Protein Antigen detection, conventional RT-PCR to Real-time RT-PCR. Real-time RT-PCR testing is an accurate and high-throughput modality and has become the standard for EVD diagnosis [86]. Current WHO guidelines recommend initial testing with an RDT when RT-PCR testing is not immediately available and to assist in triage and case management when clinical and laboratory resources are overwhelmed [87]. Furthermore, the requirement for collection and transport of venipuncture blood will continue to confer additional safety and logistical hurdles. In order to face these challenges, it is imperative that international partners work together with national health ministries to strengthen laboratory capacity in regions where Ebola is endemic, including the development of practical improvements to pre- and post-analytic processes and the training of local laboratory technicians in molecular diagnostic techniques, biosafety practices, and quality control [86].

5. Cost and effectiveness of Ebola outbreaks responses

The Ebola Response is highly complex. It requires the continuous effort by hundreds of different kinds of organizations and thousands of people to implement it quickly, effectively and efficiently [88]. Many countries all over the world have put public health measures (National response) in place to control EVD, apart from the supportive care that could be administered to patient. These measures include checking and screening for EBOV at the airports and other points of entry, quarantine of people coming from regions associated with Ebola, and isolation of suspected and clinically diagnosed

patients. The corner-stone for controlling an outbreak of EVD is to interrupt the viral transmission chain [7]. Management of survivors of EVD can also contributed to a good control of the outbreak. In the West Africa outbreak, Non-Conventional Humanitarian Interventions (NCHI) was declared as the principal strategy with major tasks at implementing relief logistics and the much-needed public health emergency responses to stamp out Ebola outbreak in vulnerable populations. The NCHI successfully supported operational containment efforts and lessons learnt in West Africa lay the foundation for accountable, transparent and innovative model for emergency response to global disease outbreaks in the most remote vulnerable populations [89]. In Uganda, Psychosocial Support (PSS) and community based volunteers in response to Ebola disease were introduced and the response was perceived to be very effective [90]. Other countries, which had experienced Ebola outbreaks before, opted to send their trained health workers to help those vulnerable regions to Ebola outbreak. For example, in August 2014 a team of 14 health workers from Uganda, which has "strong experience" of working with domestic Ebola outbreaks, had been deployed by the WHO to JFK Hospital in Monrovia, Liberia [91]. On 27 October 2014 it was announced that a further 30 Ugandan health workers were dispatched to affected countries in West Africa [92].

Various organizations around the world have always responded to all Ebola outbreaks: WHO, CDC, Medecins Sans Frontieres, etc. They work in collaboration or in association with health ministry of different countries which have been mapped out as areas with Ebola outbreaks. Special attention was taken to the West African outbreak. In August 2014, the outbreak was declared as an international public health emergency and a roadmap was published to guide and coordinate the international response to the outbreak, aiming to stop ongoing Ebola transmission worldwide within 6–9 months [93]. As of September 2014, a massive international response to the crisis was under way. The United Nations Mission for Ebola Emergency Response (UNMEER) had the task of overall planning and coordination, directing the efforts of the UN agencies, national governments, and other humanitarian actors to the areas where they are most needed [94]. UNMEER's objective was to work with others to stop the Ebola outbreak. UNMEER worked closely with governments, regional and international actors, such as the African Union (AU) and the Economic Community of West African States (ECOWAS), and with UN Member States, the private sector and civil society. Accra, in Ghana, served as a base for UNMEER, with teams in Guinea, Liberia and Sierra Leone [95, 96].

Funding is critical in responding to large and severe outbreaks of the nature of the West African Ebola outbreak. Many countries specifically donated to bring this health event under control. The US was the first country to donate to the Ebola response, then came the UK, Germany and the World Bank. The U.S. government allocated approximately $2.369 billion for Ebola response activities, including $798 million to CDC, $632 million to the Department of Defense, and $939 to the U.S. Agency for International Development. In addition to providing personnel, technical expertise, and resources to the response, these funds established three new emergency operations centers in Guinea, Liberia, and Sierra Leone [97]. Charity organizations, foundations and individuals also contributed financially to the global Ebola response.

6. Conclusion

EVD remains a global health problem. Identified in 1976 in Zaire (now Democratic Republic of Congo), Ebola is a highly contagious virus that manifests itself in the form of a hemorrhagic fever. The natural reservoir of the virus is fruit bat, which can contaminate humans directly or indirectly, through primates. Human-to-human transmission occurs through body fluids such as blood, stools, saliva, etc. The most severe Ebola outbreak began in December 2013 in south-eastern Guinea (West Africa) and extended to Liberia and Sierra Leone. The virus also affected Nigeria, Senegal, and Mali and even beyond the African continent (USA, UK, and Italy); at the end of October 2014, there were nearly 5000 deaths caused by the EVD. The latest outbreak ended on 2 July 2017, in the Likati Health Zone in Bas-Uélé Province of the Democratic Republic of the Congo (DRC).

Aside the high CFR associated with EVD (between 25 and 90%), a worrying phenomenon has been the continuous loss of already inadequate critical clinical and support workforce to the disease in outbreak and response settings. In low resource settings, the challenge has been the inability of the ministries of health to provide the adequate medical consumables necessary to protect the health workers and to ensure proper infection control practices. While health staff in these regions are gaining more knowledge and experience in dealing with occasional outbreaks, these logistical challenges considerably hinder their practice and further expose them to infections.

Though there is no effectively established drug for the treatment of EVD, recent advancement in vaccine development present a ray of hope that EVD could potentially be a vaccine preventable disease.

It is noted that Ebola outbreaks have the potential to escalate in resource-challenged regions with non-existent or very basic health infrastructure, poor road networks making the communities hard-to-reach and the primary co-existence or apparent contact with reservoirs. In the instance of the 2014 West African outbreak which was reported in densely populated urban centers, the disease spread rapidly due to weak health systems, inadequate infection prevention and control measures and non-responsive disease surveillance systems. Partnership between international organizations and ministries of health of Ebola endemic countries therefore become crucial to prevent, detect and appropriately respond to surges of Ebola among populations. This may be done through direct support to strengthen disease surveillance systems to ensure total coverage of all regions/provinces and districts, strengthening event based surveillance to establish early warning systems for disease outbreaks, building the capacity of local laboratories and encouraging the formation of a network of laboratories within and among neighboring countries while prioritizing infection prevention and control measures. Considering the ease of global spread of this disease in light of the rapid migratory patterns in recent years, the burden of preventing and controlling this disease rests on the Public health authorities of all countries over the world and their partners to work towards:

• Organizing community education campaigns designed to give more details on the viral nature of the EVD.

- Increase awareness through health education of the population through campaigns about EVD with particular attention to: hygienic measures, cooking of bush meat as long as possible, avoiding coming into contact with the biological fluids from persons suspected or diagnosed with a hemorrhagic fever.

- Communities affected by the Ebola virus must inform the population of the measures taken to contain the outbreak, including safe, dignified burial and funeral practices. People who have died from this infection must be buried quickly and without excessive risk to those who carry out the burial.

- Inform the population about the physio-pathological aspect of the virus in order to reduce rumors and false beliefs about the disease.

- Expanding training of qualified people for better management of the outbreak, and increase supply of medical materials to isolated rural areas.

- Establishing structures for early detection of any future outbreaks. Motivating the health care professionals, especially those working in the zone with previous Ebola outbreaks.

- For travelers, it is important to impose quarantine to any person suspected or diagnosed with EVD.

- Laboratory research should be carried out in biosafety. Procedures on sterilization and decontamination must be rigorously applied to avoid laboratory contamination.

Author details

Kasangye Kangoy Aurelie[1,2]*, Mutangala Muloye Guy[3,4], Ngoyi Fuamba Bona[5], Kaya Mulumbati Charles[6], Avevor Patrick Mawupemor[7] and Li Shixue[1]

*Address all correspondence to: aureliekasangye@yahoo.fr

1 School of Public Health, Social Medicine and Health Management Department, Shandong University, Jinan, Shandong, China

2 School of Public Health, University of Lubumbashi, Lubumbashi, Democratic Republic of the Congo

3 School of Medicine, Department of Obstetrics and Gynecology, Qilu Hospital, Shandong University, Jinan, Shandong, China

4 School of Medicine, Department of Obstetrics and Gynecology, University of Lubumbashi, Lubumbashi, Democratic Republic of the Congo

5 Public Health Ministry of the Democratic Republic of the Congo, Department of Epidemiology, Kinshasa, Democratic Republic of the Congo

6 School of Medicine, Department of Public Health, University of Lubumbashi, Lubumbashi, Democratic Republic of the Congo

7 School of Medical and Health Sciences, Mountcrest University College, Accra, Ghana

References

[1] WHO. Ebola Virus Disease. WHO Africa. http://www.afro.who.int/health-topics/ebola-virus-disease, 2017 WHO/Regional office for Africa

[2] Hewlett BL, Hewlett BS. Providing care and facing death: Nursing during Ebola outbreaks in Central Africa. Journal of Transcultural Nursing. 2005;**16**:2891

[3] Kangoy AK, Muloye GM, Avevor PM, Shixue L. Review of past and present Ebola hemorrhagic fever in the Democratic Republic of Congo 1976-2014. African Journal of Infectious Diseases. 2016;**10**(1):38-42

[4] Le Point international. Le découvreur belge de l'Ebola ne craint pas une épidémie majeure hors d'Afrique. http://www.lepoint.fr/monde/

[5] le monde.fr.1976, à la découverte du virus Ebola. 2014. www.lemonde.fr/planete/article/

[6] Torpiano P, Pace D. Ebola: Too far or so close? Malta Medical Journal. 2014;**26**:32-40

[7] Muyembe JJ, Mulangu S, Masumu J, Kayembe JM, et al. Ebola virus outbreaks in Africa: Past and present. The Onderstepoort Journal of Veterinary Research. 2012;**79**:1-8

[8] Netesov SV, Feldmann H, Jahrling PB, Klenk HD, Sanchez. Family Filoviridae. In: Virus Taxonomy—Seventh Report of the International Committee on Taxonomy of Viruses. San Diego, USA: Academic Press; 2000. pp. 539-548. ISBN 0-12-370200-3

[9] Pringle CR. Virus taxonomy-San Diego 1998. Archives of Virology. 1998;**143**(7):1449-1459

[10] Feldmann H, Geisbert TW, Jahrling PB, Klenk H-D, et al. Family Filoviridae. In: Fauquet CM, editor. Eighth Report of the International Committee on Taxonomy of Viruses. San Diego, USA: Elsevier/Academic Press; 2005. pp. 645-653. ISBN 0-12-370200-3

[11] Mayo MA. ICTV at the Paris ICV: Results of the plenary session and the binomial ballot. Archives of Virology. 2002;**147**(11):2254-2260

[12] Kuhn JH, Becker S, Ebihara H, Geisbert TW, et al. Proposal for a revised taxonomy of the family Filoviridae: Classification, names of taxa and viruses, and virus abbreviations. Archives of Virology. 2010;**155**(12):2083-2103. PMC 3074192 Freely accessible

[13] International Committee on Taxonomy of Viruses. Virus Taxonomy: 2013 Release. https://talk.ictvonline.org/taxonomy/

[14] Bowen ETW, Lloyd G, Harris WJ, Platt GS, et al. Viral haemorrhagic fever in southern Sudan and northern Zaire. Preliminary studies on the aetiological agent. Lancet. 1977;**309**(8011):571-573. PMID 65662

[15] http://whqlibdoc.who.int/bulletin/1978/Vol56-No2/bulletin_1978_56(2)_247-270.pdf

[16] Le Guenno B, Formenty P, Wyers M, Gounon P, Walker F, Boesch C. Isolation and partial characterisation of a new strain of Ebola virus. Lancet. 1995;**345**(8960):1271-1274. PMID 7746057

[17] Kuhn JH. Filoviruses. A compendium of 40 years of epidemiological, clinical, and laboratory studies. Archives of Virology. Supplementum. 2008;**20**:13-360. PMID 18637412

[18] Wamala JF, Lukwago L, Malimbo M, Nguku P, Yoti Z, et al. Ebola hemorrhagic fever associated with novel virus strain, Uganda, 2007-2008. Emerging Infectious Diseases. 2010;**16**(7):1087-1092. PMC 3321896 Freely accessible. PMID 20587179

[19] MacNeil A, Farnon EC, Wamala J, Okware S, et al. Proportion of deaths and clinical features in Bundibugyo Ebola virus infection, Uganda. Emerging Infectious Diseases. 2010;**16**(12):1969-1972. PMC 3294552 Freely accessible. PMID 21122234

[20] Geisbert TW, Jahrling PB. Use of immunoelectron microscopy to show Ebola virus during the 1989 United States epizootic. Journal of Clinical Pathology. 1990;**43**(10):813-816. PMC 502829 Freely accessible. PMID 2229429

[21] Leroy EM, Rouquet P, Formenty P, Souquière SF, Kilbourn A, Froment JM. Multiple Ebola virus transmission events and rapid decline of central African wildlife. Science. 2004;**303**:387-390

[22] Leroy EM, Kumulungui B, Pourrut X, Rouquet P, Hassanin A, Yaba P, Délicat A, Paweska JT, Gonzalez JP, Swanepoel R. Fruit bats as reservoirs of Ebola virus. Nature. 2005;**438**:575-576

[23] Pourrut X, Kumulungui B, Wittmann T, Moussavou G, et al. The natural history of Ebola virus in Africa. Microbes and Infection. 2005;**7**(7-8):1005-1014

[24] Morvan JM, Deubel V, Gounon P, Nakouné E, et al. Identification of Ebola virus sequences present as RNA or DNA in organs of terrestrial small mammals of the Central African Republic. Microbes and Infection. 1999;**1**(14):1193-1201

[25] Groseth A, Feldmann H, Strong JE. The ecology of Ebola virus. Trends in Microbiology. 2007;**15**(9):408-416

[26] Olival KJ, Islam A, Yu M, Anthony SJ, et al. Ebola virus antibodies in fruit bats, Bangladesh. Emerging Infectious Diseases. 2013;**19**(2):270-273

[27] CDC. Transmission of Ebola Virus; 2015. https://www.cdc.gov/vhf/ebola/transmission/index.html

[28] Biek R, Walsh PD, Leroy EM, Real LA. Recent common ancestry of Ebola Zaire virus found in a bat reservoir. PLoS Pathogens. October 2006;**2**(10):e90, 0885-0886

[29] Organisation Mondiale de la Santé (OMS). Ce que l'on sait à propos de la transmission interhumaine du virus Ebola : Évaluation de la situation; 2014. http://www.who.int/mediacentre/news/ebola/06-october-2014/fr/

[30] WHO. Ebola Virus Disease. Fact Sheet No 103. Disease Fact Sheets [Internet]. 2014. http://www.who.int/mediacentre/factsheets/fs103/en

[31] Rambaut A. Case fatality rate for ebolavirus. Epidemic; 2014. http://epidemic.bio.ed.ac.uk/ebolavirus_fatality_rate

[32] Walsh PD, Abernethy KA, Bermejo M, Beyers R, De Wachter P, et al. Catastrophic ape decline in western equatorial Africa. Nature. 2003;**422**:611-614

[33] Ebola Situation Report (PDF). World Health Organization. 21 January 2015. Retrieved 22 January 2015. http://apps.who.int/iris/bitstream/10665/149314/1/roadmapsitrep_21Jan2015_eng.pdf?ua=1

[34] Reuters. Mali Confirms New Case of Ebola, Locks Down Bamako Clinic. 12 November 2014. Retrieved 15 November 2014. https://in.reuters.com/article/health-ebola-mali/update-1-mali-confirms-new-case-of-ebola-locks-down-bamako-clinic-idINL6N0T15CN20141112

[35] WHO. Ebola Response Roadmap Situation Report Update. World Health Organization. 7 November 2014. Retrieved 7 November 2014. http://apps.who.int/iris/bitstream/10665/137592/1/roadmapsitrep_7Nov2014_eng.pdf?ua=1

[36] WHO. Ebola Response Roadmap – Situation Report. World Health organization. 31 December 2014. Retrieved 1 January 2015. The reported case fatality rate in the three intense-transmission countries among all cases for whom a definitive outcome is known is 71%. http://apps.who.int/ebolaweb/sitreps/20141231/20141231.pdf

[37] WHO. Ebola Virus Disease – Italy. WHO. http://www.who.int/csr/don/13-may-2015-ebola/en/

[38] Una enfermera que atendió al misionero fallecido García Viejo, contagiada de ébola (in Spanish). El Mundo. 6 October 2014. Retrieved 6 October 2014. http://www.elmundo.es/madrid/2014/10/06/5432bb62e2704e347a8b4577.html?a=a733fe5654cd56f5e1d50d769a9b4204&t=1412616936

[39] Ebola Outbreak Situation Report (PDF). WHO. 8 October 2014. Retrieved 15 October 2014. http://apps.who.int/iris/bitstream/10665/136020/1/roadmapsitrep_8Oct2014_eng.pdf?ua=1

[40] Ebola Virus Epidemic Situation Map, Simplified. 2014. https://en.wikipedia.org/wiki/West_African_Ebola_virus_epidemic#/media/File:2014_ebola_virus_epidemic_in_West_Africa_simplified.svg

[41] WHO Ebola Response Team. Ebola virus disease in West Africa – The first 9 months of the epidemic and forward projections. New England Journal of Medicine. 23 September 2014;**371**:1481-1495

[42] West Africa Outbreak. Centers for Disease Control and Prevention. 2014. Retrieved 11 April 2015. https://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/previous-updates.html

[43] WHO Director-General Briefs Media on Outcome of Ebola Emergency Committee. World Health Organization. Retrieved 2 April 2016. http://www.who.int/csr/disease/ebola/guinea-flareup-update/en/

[44] WHO. Interim Advice on the Sexual Transmission of the Ebola Virus Disease. World Health Organization. Retrieved 28 October 2016. http://www.who.int/reproductivehealth/topics/rtis/ebola-virus-semen/en/

[45] WHO Director-General Addresses the Executive Board. World Health Organization. Retrieved 27 January 2016. http://www.who.int/csr/disease/ebola/response/en/

[46] Ebola Data and Statistics. World Health Organisation. Retrieved 9 June 2016. http://apps.who.int/gho/data/view.ebola-sitrep.ebola-summary-latest?lang=en

[47] Ebola Situation Report. Ebola Data and Statistics. World Health Organization. 12 January 2015. Retrieved 28 January 2015. http://apps.who.int/gho/data/view.ebola-sitrep.ebola-summary-20150112?lang=en

[48] Identification of Ebola Virus on Firefly Dx. http://psidcorp.com/system/files/media/GenArraytion%20Ebola%20Assay%20on%20Firefly%20Dx.pdf

[49] WHO Declares Nigeria Ebola-Free. WHO. Retrieved 22 July 2016. http://www.afro.who.int/media-centre/news

[50] Diseases – Activity 1 – Glossary, page 3 of 5. science.education.nih.gov. Retrieved 2010-11-03

[51] WordNet Search – 3.0. Princeton University. wordnetweb.princeton.edu. Retrieved 3 November 2010. http://wordnetweb.princeton.edu/perl/webwn?s=index%20case

[52] Sporadic STEC O157 Infection: Secondary Household Transmission in Wales. USA: Centers for Disease Control and Prevention. www.cdc.gov. 1 January 1994. Retrieved 3 November 2010

[53] WHO. Ebola hemorrhagic fever in Zaire. Bulletin of the World Health Organization. 1979;**56**:271-293

[54] Leroy EM, Epelboin A, Mondonge V, Pourrut X, et al. Human Ebola outbreak resulting from direct exposure to fruit bats in Luebo, Democratic Republic of Congo. Vector-Borne and Zoonotic Diseases. 2007;**9**:723-728

[55] Georges AJ, Leroy EM, Renaud AA, et al. Ebola hemorrhagic fever outbreaks in Gabon, 1994-1997: Epidemiologic and health control issues. Journal of Infectious Diseases. 1999;**179**:S65-S75

[56] WHO. Ebola haemorrhagic fever – South Africa [469 KB, 8 pages]. Weekly Epidemiological Record. 1996;**71**(47):359

[57] Okware S, Omaswa FG, Zaramba S, Opio A, Lutwama JJ, Kamugisha J, Rwaguma EB, Kagwa P, Lamunu M. An outbreak of Ebola in Uganda. Tropical Medicine & International Health. 2002 Dec;**7**(12):1068

[58] Bwaka MA, Bonnet MJ, Calain P, Colebunders R, De Roo A, Guimard, et al. Organization of patient care during the Ebola hemorrhagic fever epidemic in Kikwit, Democratic Republic of the Congo, 1995. Journal of Infectious Diseases. 1 February 1999; **179**(Supplement_1):S268-S273

[59] Okware S. Managing Ebola in low-resource settings: Experiences from Uganda. Medicine, Infectious Diseases, Ebola; August 2016. https://www.intechopen.com/books/ebola/managing-ebola-in-low-resource-settings-experiences-from-uganda

[60] Finding Ebola's 'patient zero'. The Guardian. Retrieved 28 November 2014

[61] Hollow tree in Guinea was Ebola's Ground Zero, scientists say. Mail & Guardian Africa. AFP. 30 December 2014. Retrieved 1 January 2016

[62] Grady D, Fink S. Tracing Ebola's breakout to African 2-year-old. The New York Times. Retrieved 11 April 2015

[63] Stylianou N. How world's worst Ebola outbreak began with one boy's death. BBC News. 27 November 2014. Retrieved 11 April 2015

[64] Maganga D, Kapetshi J, Berthet N, Kebela Ilunga B, et al. Ebola virus disease in the Democratic Republic of Congo. The New England Journal of Medicine. 2014;**371**:2083-2091

[65] WHO. External Situation Report 1. Regional Office for Africa. Ebola Virus Disease– Democratic Republic of the Congo. World Health Organization. 15 May 2017. Retrieved 16 May 2017. http://apps.who.int/iris/handle/10665/255713?locale=en

[66] Garrett L. The Coming Plague: Newly Emerging Diseases in a World Out of Balance. London: Virago Press; 1994. pp. 100-105. ISBN 1-86049-211-8

[67] WHO. Health Worker Ebola Infections in Guinea, Liberia and Sierra Leone. May 2015. http://www.who.int/csr/resources/publications/ebola/health-worker-infections/en/

[68] Grinnell M, Dixon MG, Patton M, Fitter D, et al. Ebola virus disease in health care workers. CDC Morbidity and Mortality Weekly Report. October 2, 2015;**64**(38):1083-1087

[69] Hero nurse Pauline Cafferkey could have contracted deadly Ebola at Christmas Day service. The Telegraph. 30 December 2014

[70] Grady D. Ebola is Diagnosed in Texas, First Case Found in the U.S. The New York Times/ Health. Sept. 30, 2014. https://www.nytimes.com/2014/10/01/health/airline-passenger-with-ebola-is-under-treatment-in-dallas.html

[71] Gidda M. Fear and Rumors Fueling the Spread of Ebola. Time Health 2014 / Infectious disease. http://time.com/3092855/ebola-fear-rumors/

[72] Mupapa K, Massamba M, Kibadi K, Kuvula K, et al. Treatment of Ebola hemorrhagic fever with blood transfusions from convalescent patient. Journal of Infectious Diseases. 1999;**179**(Supplement 1):S18-S23

[73] Gupta M, Mahanty S, Bray M, Ahmed R, Rollin PE. Passive transfer of antibodies protects immunocompetent and imunodeficient mice against lethal Ebola virus infection without complete inhibition of viral replication. Journal of Virology. 2001;**75**:4649-4654. PMID:11312335

[74] Oswald WB, Geisbert TW, Davis KJ, Geisbert JB, et al. Neutralizing antibody fails to impact the course of Ebola virus infection in monkeys. PLoS Pathogens. January 2007;**3**(1):e9, 0062-0066

[75] Ebola Virus Infection Treatment & Management. Updated: Jun 03, 2016. http://emedicine.medscape.com/article/216288-treatment#d9

[76] Richardson JS, Dekker JD, Croyle MA, Kobinger GP. Recent advances in Ebolavirus vaccine development. Human Vaccines. 2010;**6**(6):439-449

[77] Henao-Restrepo AM et al. Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: Final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!). The Lancet. 2016;**389**(10068):505-518. PMID 28017403. Retrieved 27 December 2016

[78]   Berlinger J. Ebola vaccine gives 100% protection, study finds. CNN. Retrieved 27 December 2016

[79]   Morvan JM, Nakouné E, Deubel V, Colyn M. Forest ecosystems and Ebola virus. Bulletin de la Société de Pathologie Exotique. 2000;**93**(3):172-175

[80]   Diallo B. Ebola en Guinée: l'ONG Plan-Guinée craint une aggravation de l'épidémie. 2014. Africaguinée.com. Available from: http://africaguinee.com/articles/2014/03/30/ebola-en-guinee-l-ong-plan-guinee-craint-une-aggravation-de-l-epidemie

[81]   Feldmann HK, Geisbert TW. Ebola haemorrhagic fever. The Lancet. 2011;**377**(9768):849-862

[82]   Leroy EM, Gonzalez JP, Baize S. Ebola and Marburg haemorrhagic fever viruses: Major scientific advances, but a relatively minor public health threat for Africa. Clinical Microbiology and Infection. 2011;**17**(7):964

[83]   de Wit E, Feldmann H, Munster VJ. Tackling Ebola: New insights into prophylactic and therapeutic intervention strategies. Genome Medicine. 2011;**3**(1):5

[84]   Lefebvre A, Fiet C, Belpois-Duchamp C, Tiv M, Astruc K, Aho Glele LS. Case fatality rates of Ebolavirus diseases: A meta-analysis of World Health Organization data. Médecine et Maladies Infectieuses. 2014;**44**(9):412

[85]   Medical Xpress. New scoring system predicts Ebola severity. February 2, 2017. https://medicalxpress.com/news/2017-02-scoring-ebola-severity

[86]   Broadhurst MJ, Brooks TJG, Pollock NR. Diagnosis of Ebola virus disease: Past, present, and future. Clinical Microbiology Reviews. 1 October 2016;**29**(4):773-793

[87]   World Health Organization. Interim Guidance on the Use of Rapid Ebola Antigen Detection Tests. Geneva, Switzerland: World Health Organization; 2015. http://www.who.int/csr/resources/publications/ebola/ebola-antigen-detection/en/

[88]   Global Response to Ebola. https://ebolaresponse.un.org/

[89]   Talla M, Chidiebere UE, Olalubi OA, Wurie I, Jonhson JK, Ngogang JY, Tambo E. Effectiveness of non-conventional humanitarian responses on Ebola outbreak crisis in West Africa. Journal of Pharmacovigilance. 2015;**3**(4):98

[90]   Thormar SB. Evaluation of Ebola Response-Uganda 2012. Feb 2013. www.adore.ifrc.org/Download.aspx?FileId=42478&.pdf

[91]   WHO. Ugandan Team Brings Ebola Experience to Liberia. World Health Organization. August 2014. http://www.who.int/features/2014/ugandan-ebola-team/en/

[92]   Uganda sends more medical personnel to Ebola-hit West Africa. Shanghai Daily. 27 October 2014. http://www.shanghaidaily.com/article/article_xinhua.aspx?id=249178

[93]   Ebola 'threat to world security'- UN Security Council. BBC News. 18 September 2014. Retrieved 18 September 2014

[94] WHO warns Ebola response could cost $1B. The Hill. 16 September 2014. Retrieved 16 September 2014

[95] UN Mission for Ebola Emergency Response (UNMEER). United Nations. Retrieved 4 October 2014. http://ebolaresponse.un.org/un-mission-ebola-emergency-response-unmeer

[96] WHO welcomes decision to establish United Nations Mission for Ebola Emergency Response. Time. EIN Presswire. 19 September 2014. https://www.einnews.com/pr_news/224890550/who-welcomes-decision-to-establish-united-nations-mission-for-ebola-emergency-response

[97] CDC. Cost of the Ebola Epidemic. https://www.cdc.gov/vhf/ebola/pdf/impact-ebola-economy.pdf